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EXPLANATORY LIST OF ABBREVIATED NAMES OF U.S.S.R. INSTITUTIONS, JOURNALS, ETC., APPEARING IN THIS TEXT

Abbreviation	Full name (transliterated)	Translation
AMN SSSR	Akademiya Meditsinskikh Nauk SSSR	Academy of Medical Sciences of the USSR
AN SSSR	Akademiya Nauk SSSR	Academy of Sciences of the USSR
GIZ BSSR	Gosudarstvennoe izdatel'stvo Belorusskoi SSR	State Publishing House of the Belorussian SSR
IEM	Institut eksperimental'noi meditsiny (Akademii Meditsinskikh Nauk SSSR)	Institute of Experimental Medicine of the Academy of Sciences of the USSR
Medgiz	Gosudarstvennoe izdatel'stvo meditsinskoi literatury	State Publishing House of Medical Literature
NIIIAM	Nauchno-issledovatel'skii ispytatel'nyi institut aviatsionnoi meditsiny	Scientific Research Testing Institute of Aviation Medicine
VMA	Voenno-meditsinskaya akademiya	Military Medical Academy
VMMA	Voenno-morskaya meditsinskaya akademiya	Naval Medical Academy
VMOLA	Voenno-meditsinskaya akademiya ordena Lenina im. S. M. Kirova	Military Medical "Order of Lenin" Academy im. S. M. Kirov
VMS	Voenno-morskie sily	Navy
VNIIA	Vsesoyuznyi nauchno-issledovatel'skii institut antibiotikov	All-Union Antibiotics Scientific Research Institute
ZhRKhO	Zhurnal Russkogo Khimicheskogo Obshchestva	Journal of the Russian Chemical Society

INTRODUCTION

The third collection of "The Effect of the Gas Medium and Pressure on Body Functions" contains the results of further work-up of the problem of the effect on the body of increased and reduced total and partial pressures of various gases in ordinary air, as well as artificial gas mixtures used in deepwater descents. A characteristic feature of this collection is the major place accorded to investigations on problems associated with being under conditions of increased pressure. Specifically, the majority of articles in this collection contain material on the study of caisson disease phenomena, which are among the most dangerous consequences of increased pressure on the body and for many decades have interfered with man's exploration of the deep.

Tremendous progress has been made in exploration of great depths in the last 40 years, due mainly to the work of Haldane and his co-workers. Taking the physical phenomenon of super saturation of fluids with gases as a basis, he determined the permissible supersaturation coefficient as applied to coming out from under pressure and introduced the concept of time and dynamics of nitrogen saturation and desaturation of various body tissues. From this he calculated and substantiated decompression regimes necessary to prevent caisson disease in divers emerging from depths as low as 30 and then 62 m. In a pressure chamber, and then in practical underwater descents, he further checked and clarified the coefficients and conditions for the dives, chiefly empirically. The decompression routines he suggested eliminated completely the occurrence of caisson disease in divers and gave a powerful impetus to the development of diving practice.

A group of scientific workers headed by Academician L. A. Orbeli greatly contributed to this work. On the basis of Haldane's statements about supersaturation coefficient and time of nitrogen desaturation of the tissues, the Soviet scientists worked out routines for safe descents to depths of 100 m with the use of air. In order to avoid the toxic effects of nitrogen and oxygen, deeper descents were made using artificial gas mixtures with reduced percentages of oxygen and helium replacing the nitrogen; thereby great practical progress was achieved. The group's main initial task was making possible increased depth of descent, and the conditions for this were worked out empirically for the most part: the limits of permissible supersaturation were determined in a pressure chamber and during practical underwater descents with respect to the occurrence of precursors of decompression disorders in man. Therefore, despite the exceptional practical achievements, the theoretical work-up of the problem was inadequate, and remains so.

The next work period of our group was given over to a manifold, detailed theoretical investigation and determination of some rules and regulations which are of great importance for diving practice. The prime

problems were: determining the exact supersaturation coefficients for various fluids and gases, and the significance of regularities found in caisson disease; elaborating precise terminology defining concepts of limiting, permissible and safe supersaturation; and resolving whether supersaturation is determined by the ratio of the tension of the indifferent gas to the total pressure after decompression or by the difference between these magnitudes. One of the papers of this series, written by A. P. Brestkin, was included in the second collection of "The Effect of the Gas Medium and Pressure on Body Functions."*

Along with the determination of the coefficients and periods of saturation and desaturation of various tissues, the important question arose of the physiological effects of gas bubbles (which are the cause of caisson disease) on the various body functions. It remained for us to determine where gas formation primarily occurs in the body, the fate of the gas bubbles formed, respiratory and circulatory reactions to the bubbles and their significance in the body's fight against caisson disease, and finally, whether or not it is possible to increase body resistance to decompression disorders.

Diving practice shows that safety of decompression conditions depends to a considerable degree on the temperature conditions during the diver's stay below and during decompression.

Also included in this collection is an article by Z. S. Gusinskii and A. I. Shvarev describing a particular case of caisson disease phenomena and the elimination of their consequences.

Finally, the collection includes a paper by B. A. Nessirio in which data is presented on the unique training given for conditions of underwater work.

The results of our group's active work-up of the problem of the toxic effect of oxygen have an important place in the collection. In contrast to the phenomena of caisson disease the toxic effect of oxygen was determined scientifically by P. Ber under laboratory conditions. Therefore, the study of its effect on the body was experimental and of a theoretical nature from the very beginning. The literature on the subject is represented by many sources, most of which deal with the mechanism of oxygen-induced convulsions and the local effect of oxygen on the pulmonary epithelium. At the same time, of great theoretical interest and practical significance are the various functional changes in divers when the oxygen effect is not accompanied by convulsions.

The question of the mechanical effect of sharp drops in pressure is new to our collections. In the article by V. N. Zvorykin, A. A. Koreshkov and P. A. Mal'kov a study was made of the reflex effects of increased pressure in the gastrointestinal tract on the respiratory and circulatory functions. This phenomenon occurs when a person is rapidly elevated, and it therefore is of undoubted significance for aviation. In the case of underwater descents with self-contained breathing apparatuses, a rapid rise to the surface is connected with excessive increase in pulmonary pressure and rupture of the alveoli. Until recently, this phenomenon, not uncommonly encountered in practice, was practically uninvestigated experimentally, as a result of which conditions for the occurrence of pressure trauma and the mechanism of the associated functional disorders were not clarified, and measures for eliminating them were not substantiated. The three papers by Yu. M. Polumiskov included in the present collection fill this gap to a certain degree. The late manifestation of pressure trauma

* Funktsii organizma v usloviyakh izmenennoi gazovoi sredy.

to the lungs and the favorable results of the therapeutic recompression used are of theoretical and practical interest.

The other articles in the collection are separate papers, most of them continuations and developments of the study published in the first two collections. Particularly noteworthy are the articles by B. A. Vinokurov and Zan Dok Men, illustrating the very different conditions of higher nervous activity during extreme rarefaction of the atmosphere in accordance with the biological significance of the unconditioned stimulus and the conditioned reflexes worked out on its basis, and papers by P. V. Oblapenko in which a fine physiological analysis of the body's reactions to unusual respiratory conditions — increased air or oxygen pressure in the respiratory tract — is presented.

Aside from their definite theoretical significance, this data is of direct practical interest for aviation.

M. P. Brestkin

N66-17127

A. I. Aleksandrov and A. P. Brestkin

THE PERMISSIBLE SUPERSATURATION COEFFICIENTS IN HUMAN BEINGS BREATHING AIR AND A HELIUM-OXYGEN MIXTURE

(O koeffitsientakh dopustimogo peresyshcheniya u lyudei pri dykhanii vozdukhom i gelio-kislorodnoi smes'yu)

It has been determined (Brestkin, 1958) that nitrogen forms more stable supersaturated liquid solutions than helium. Thus, in nitrogen-water solutions the supersaturation coefficient (SC) varies from 4.11 to 4.56; in helium-water solutions, from 2.03 to 2.43. In this connection it was interesting to determine the permissible supersaturation coefficient (PSC) in human beings breathing air and a helium-oxygen mixture.

Our investigation is of definite practical, as well as theoretical significance, since the PSC underlies the calculation of the decompression conditions. At the time of our experiments in 1950 there was no experimental data in the literature on PSC values in human beings breathing a helium-oxygen mixture. The values of the PSC used in calculations of deepwater helium-oxygen decompression conditions were determined mathematically by the results of practical descents by divers to great depths, and should therefore be regarded as arbitrarily calculated figures.

Method

The values of the PSC were determined in eight professional divers, from 20 to 26 years of age, and in the authors of this work, 28 and 38 years old. The investigation was made in a large pressure chamber. Four subjects participated simultaneously in the same experiment.

The subjects were given an indifferent gas at a given pressure for 6 hrs. At the end of this time, which was considered adequate for 100% saturation of the body with gas, the pressure in the chamber was reduced to normal for 1 min. During the next 18 hrs the subjects were under observation in a pressurized laboratory. If no symptoms of decompression sickness occurred in them, after 3 days a similar experiment was performed with a pressure of 1.5 m of water above the previous.

Such a gradual increase in pressure from experiment to experiment was continued until one of the subjects showed distinct signs of caisson disease after decompression. The value of the pressure in this latter case was considered the limiting pressure for the subject. With the occurrence of severe signs of decompression sickness, the subject immediately was subjected to therapeutic recompression. The therapeutic recompression was conducted even when mild but persistent symptoms occurred.

The PSC was calculated from the following formula:

$$\text{PSC} = \frac{P_{tot} \cdot n}{100 \cdot 1} = \frac{P_0}{1}$$

where P_{tot} is the total limiting pressure in atmospheres, i.e., after a six-hour period at this pressure the subject developed signs of decompression sickness;

n is the percentage of the indifferent gas in the inhaled air;

P_0 is the tension of the indifferent gas in the body tissues, which was numerically equal to its partial pressure in the inhaled gas mixture after a six-hour period under pressure, that is, equal to $\frac{P_{tot} \cdot n}{100}$; and

1 is the ambient pressure in atm after decompression.

Before the experiment the chamber was half-filled with water, ranging in temperature from 11 to 14°. During the experiment the subjects, dressed in warm underwear and diving suits, sat up to their chests in water for the entire 6 hours, without doing any work. On observance of standard experimental conditions, each subject breathed through the mouthpiece of the light diving apparatus in both the helium-oxygen gas-mixture and air experiments. These apparatuses were filled from a transportable tank through a collector with bypasses.

To keep the composition of the inhaled air constant, the subjects replaced the gas mixture in the breathing bag of the apparatus once every 5 min. Gas-mixture composition was checked by analysis of gas samples on a Haldane apparatus; these samples were taken from the breathing bags every 15 min. Usually the oxygen content of the breathing mixture ranged from 21 to 18%; that of nitrogen and helium, from 79 to 82%.

Every 3 hrs the subjects substituted the apparatuses for several seconds, because with longer use the chemical absorbent may not completely remove the carbon dioxide from the breathing mixture.

Results of the Experiments

According to the data given in the table, the limiting pressure on breathing air was 2.95 atm for all 8 subjects. After a 6 hour stay under this pressure all subjects developed severe itching of the skin; In addition, joint pains occurred in two subjects 10 and 15 hrs after decompression. Therapeutic recompression was performed on one of the patients. Therefore, it may be considered that the PSC of nitrogen* is $\frac{2,95 \cdot 81.4}{100 \cdot 1} = 2.40$, where 81.4 is the nitrogen content of the inhaled air in percent (according to an analysis of the breathing-apparatus sample).

On breathing the helium oxygen mixture the limiting pressure in three subjects was equal to 3.25 atm. Shortly after coming out from under pressure they complained of severe joint pains, but skin itchiness was absent; objectively they showed dyspnea and sweatiness. Therapeutic

* For convenience of presentation, the PSC on breathing air will be called the PSC of nitrogen, that on breathing helium-oxygen mixture, the PSC of helium.

recompression was performed on two of them. The other five subjects showed no signs of decompression sickness, and evidently for them the limiting pressure was somewhat more than 3.25 atm. However, we refrained from using any further pressure increase because of the possible occurrence of severe symptoms of decompression sickness. Therefore, the PSC of helium is equal to $\frac{3.25 \cdot 82}{100} = 2.66$, where 82 is the helium content in the breathing mixture in percent.

Experimental data for determining the PSC

Pressure		Number of subjects	Partial pressure of indifferent gas (in atm)	Cases of occurrence of decompression symptoms
in m of water	in atm.			
On breathing air				
12.5	2.25	5	1.78-1.86	Absent
14.0	2.40	2	1.90	"
15.5	2.55	2	2.01	"
16.5	2.65	2	2.08	"
18.0	2.8	6	2.21-2.32	2 (itching of the skin)
19.0	2.95	8	2.36-2.40	8
On breathing the helium-oxygen mixture				
12.5	2.25	8	1.91-2.02	Absent
14.0	2.40	4	1.86	"
15.5	2.55	4	2.09	"
16.5	2.65	4	2.13	"
18.0	2.8	4	2.33	"
19.5	2.95	4	-	"
21.0	3.10	4	2.46	"
22.5	3.25	8	2.65-2.67	3

The values established for the PSC characterize resistance of the subjects to decompression sickness under conditions of a 6 hour stay under pressure in cold water without physical exertion.

Discussion of Results

As shown by the results given in the table, the PSC of helium is greater than that of nitrogen, whereas, according to the data of A. P. Brestkin indicated above (1958) the SC of nitrogen is greater than that of helium.

The question arises as to why nitrogen, which forms more stable supersaturated solutions with fluids, has a lower PSC value than helium. This discrepancy is explained chiefly by the fact that the SC and PSC are different in their nature. As is well known, the SC is the ratio of the tension of an indifferent gas in solution to the ambient pressure at which the first gas bubbles are formed, whereas the PSC is the ratio of the

tension of the indifferent gas in the body tissues to the ambient pressure at which the first signs of decompression sickness occur.

The classical experiments of N. I. Pigorov (1852) and V. V. Pashutin (1881) with the injection of air into the blood vessels of dogs indicate convincingly that the bubbles of an indifferent gas formed in the body in small quantities fail to produce any functional disorders, and are readily eliminated by the body. The mechanism of elimination of the free indifferent gas from the blood stream was analyzed by A. P. Brestkin (1954). This data indicates that signs of decompression sickness occur only when a relatively large quantity of free indifferent gas is formed, which the body can eliminate only with great difficulty or cannot eliminate at all without the timely use of therapeutic recompression.

Therefore, the PSC is a more complicated parameter than the SC of gas-fluid solutions and characterizes not only the properties of body tissues and primarily those of the blood for maintaining a dissolved indifferent gas in a supersaturated state, but also the capacity of the organism for eliminating the gas bubbles formed. Naturally, the rate of elimination of the free indifferent gas should be determined both by the condition of the compensatory mechanisms of the body, and by the nature of the gas.

Because nitrogen dissolves better than helium, with the same degree of rapid pressure reduction, a greater excess of indifferent gas is formed in the body of a diver breathing air than when breathing a helium-oxygen mixture. Evidently, the volume of the free gas produced in the first case will be greater than in the second.

In addition, the process of elimination of the free indifferent gas from the body of the diver through the lungs and partly through the skin depends not only on its quantity but also on its power of diffusion. According to the Exner rule (Exner, 1875), the diffusion coefficient of helium is much greater than that of nitrogen. Therefore, with the same pressure reduction the body more readily eliminates helium bubbles than nitrogen bubbles, since the free helium is formed in a smaller quantity and diffuses rapidly.

Evidently, the same circumstance explains the discrepancy indicated in the relations between the figures for the SC and the PSC for nitrogen and helium. The possibility has not been ruled out that even in the diver's body the gas bubbles formed on breathing a helium-oxygen mixture have lower degrees of supersaturation than on breathing air, despite the fact that the PSC of nitrogen is less than that of helium. The considerations expressed here about the SC and PSC agree with data of the extensive and very convincing studies of P. M. Gramenitskii and others (1964) as well as with the data of G. L. Zal'tsman and I. D. Zinov'eva (1964) on the PSC determination in human beings after breathing air and a helium-oxygen gas mixture for an hour, under pressure in a dry pressure chamber.

Conclusions

1. Under conditions of a pressure chamber half-filled with water, the value of the PSC on breathing air is equal to 2.40; on breathing a helium-oxygen gas mixture, 2.66.

2. The higher value of the PSC on breathing the helium-oxygen gas mixture is evidently explained by the fact that the body more readily eliminates the helium bubbles, since this gas possesses a higher diffusion coefficient.

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A. P. Brestkin

RELATIONSHIP BETWEEN THE SUPERSATURATION COEFFICIENT OF GAS- LIQUID SYSTEMS AND THE TENSION OF DISSOLVED GAS

(Zavisimost' koeffitsienta peresyshcheniya sistem gaz- zhidkost' ot napryazheniya rastvorennogo gaza)

It has been noted (Haldane and Priestley, 1937) that the permissible saturation coefficient (PSC) for divers decreases with increased depth of descent and time spent at the bottom, i.e., with increase in the parameters determining the tension of an indifferent gas in the body tissues. Evidently, such a reduction in the PSC is connected not only with functional changes of the body but also with change of the capacity of the tissues for retaining the dissolved indifferent gas in a state of supersaturation. In this connection, it was very interesting to study the relationship between the tension of the dissolved gas and the supersaturation coefficient (SC) of the solution, the value of which also characterizes the capacity of the fluid for retaining the dissolved gas in a supersaturated state.

Method

The study consisted of two series of experiments: in the first a study was made of supersaturated gas-fluid solutions in the pressure range from 1 to 8 atm; in the second, from 10 to 200 atm. The experiments were performed with two fluids (water and benzene) and with three gases (helium, nitrogen, and carbon dioxide).

1. Experiments with pressures from 1 to 8 atm were performed with an apparatus already used by us (Brestkin, 1958). A water thermostat with a saturator and dilatometer placed on it were put in the pressure chamber, where the experimenter and an assistant were located during the experiment. A rheostat and mercury relay were placed outside the chamber, and the electric wires coming from them into the electric heater and heat regulator of the water thermostat were introduced into the chamber through a connecting pipe with an asbestos stuffing box.

The water in the thermostat was mixed with air passed from a steel tank through a glass tube with a large number of holes. All preparatory work for the experiment, including filling the saturated fluid with gas, was done outside the chamber. The necessary pressure in the chamber was created with compressed air and measured carefully with a calibrated manometer. Saturation of the fluid with gas at the necessary pressure P_0

was accomplished by vigorous shaking of the saturated fluid by hand for 10 min. A specially performed experiment showed that this period was more than adequate for reaching complete saturation. Without changing the pressure in the chamber, the fluid saturated with gas was transferred to the dilatometer, thus creating a slight excess gas pressure in the saturator by means of a mercury U-tube. Thereby precautionary measures were taken to insure that the solution in the dilatometer be free of gas bubbles.

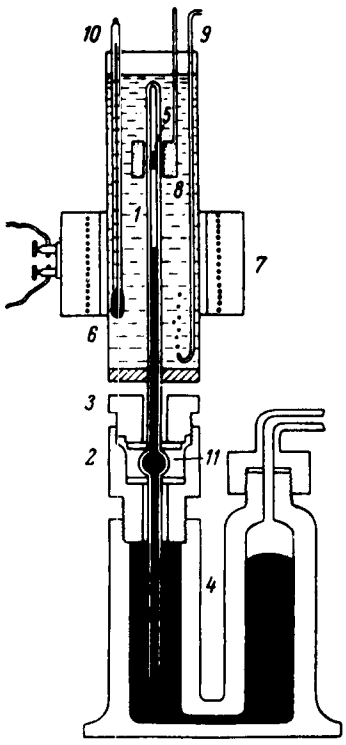


FIGURE 1. Apparatus for investigation of supersaturated gas-fluid solutions at high pressures (Explanation in the text)

The dilatometer filled with solution was disconnected from the apparatus and fixed in the thermostat. To dissolve the very slight traces of free gas which might be found between the wall of the dilatometer and the solution, the pressure in the chamber was increased by 2-3 atm. During this time, the experimenters were in an antechamber at a lower pressure in order to avoid excess nitrogen accumulation in their bodies. At the end of 30 min the pressure in the chamber was reduced to a figure at which gas bubble formation in the investigated supersaturated solution began to be observed. The pressure in the antechamber was also brought up to this figure; the experimenters again went into the chamber and observed the test solution.

After initial reduction of pressure by 25-50% it was further reduced by sudden drops at intervals of 0.2-0.5 atm. The period of observation of the solution at each pressure was 20 min. As a result, the pressure P was found, at which the first gas bubble was formed in the supersaturated solution in a period of 20 min. Every experiment was repeated 2-4 times. From the data of parallel experiments the average figure of P, the value of $SP = \frac{P_0}{P}$, and the difference $P_0 - P$ were calculated. Variations of P from the average figure did not exceed 10%. The experimental data obtained is presented in the table, in which, for the purposes of comparison, the values of SP are given for a pressure of 1 atm, taken from our previous work (Brestkin, 1958).

2. Experiments with pressures from 10-200 atm were performed with a Cailletet apparatus, which we modified somewhat (Figure 1). The main part of this instrument is a glass barometer tube (1). We used tubes about 50 cm long with outside diameters of 10-12 mm and inner diameters of 1-4 mm. The upper end of the tube was fused in the form of a hemisphere;

the lower end was left open. For 25 cm from the upper sealed end divisions were made on the tube at 1 mm intervals. At a distance of 8- 12 cm from the lower open end a bulb was blown out (11) for the purpose of attaching the glass tube in the steel connecting pipe (2). The glass tube prepared in this way was carefully calibrated with mercury, enabling accurate determination of the volume between the divisions inscribed and of the entire tube as a whole.

The glass tube was fixed in a steel connecting pipe (2) by means of portland cement, two rubber washers and a clamping sleeve (3). After the cement hardened, a certain quantity of fluid and an iron rod (5) soldered into a glass capillary were introduced into the barometer. The entire remaining volume of the tube was filled with the gas being studied. For the purpose of introducing fluid into the glass tube, we prepared a small funnel with a long and very fine capillary, which passed freely into the tube up to its sealed end. A quantity of fluid was introduced, sufficient to dissolve all the gas filling the residual volume of the tube at pressures up to 250 atm and at temperatures at which the studies were made. The tube was filled with the investigated gas through the same capillary by blowing the gas through it for a long time. In order to avoid evaporation of the fluid in the tube in this process it was frozen with dry ice.

The open end of the tube was then sealed with a rubber stopper and immersed in a cup of mercury. The stopper was removed under the layer of mercury, and a short test tube of mercury was set on the end of the tube, thereby forming a mercury valve.

The connecting pipe with the filled glass tube was screwed on to a steel buffer (4), and in the apparatus thus assembled the pressure was immediately raised by forcing in oil with an ordinary press. The mercury was squeezed into the tube from the buffer, compressing the gas. During the screwing of the instrument and the increase of pressure in it, the end of the tube with the fluid was constantly cooled with dry ice. Freezing the fluid was necessary so that when the tube was turned in a vertical position the fluid and iron rod (5) in it remained in the upper portion.

To maintain the necessary temperature in the tube (1) a special thermostat was set on it. A glass cover (6) about 5 cm in diameter and about 50 cm long was placed on the tube by means of a large rubber stopper. The cover was filled with water, which was heated to the necessary temperature with a tube electric furnace (7). The furnace was supplied with rheostats which kept the temperature in the cover constant. The water was mixed with air coming into the cover from the tank through a reducer, rubber tube and metal tube (9). The water temperature was measured with shortened precision mercurial thermometers (10).

After establishing the necessary temperature in the thermostat, the pressure at which the quantity of investigated gas completely dissolved in the given fluid was determined. For most rapid solubilization the gas was mixed with the fluid with a mixer (5) driven by a special magnet (8). The magnet fit readily into the cover and had a hole through which the barometer tube (1) passed freely.

During this mixing process the pressure in the tube was periodically raised until the last very small gas bubble disappeared. The pressure P_0 corresponding to the point of complete solubilization was recorded in the table.

After determination of this point the pressure was raised another 10 atm and left unchanged for 20—50 min in order to be absolutely sure that there were no traces of undissolved gas.

At the end of this period the pressure in the tube was reduced by intervals of 5 atm, converting the saturated solution into a supersaturated one. To avoid shaking the supersaturated solution the pressure was reduced very cautiously, and during this time the magnet was removed completely from the cover. After each pressure reduction a 20 minute observation was made of the supersaturated solution. The pressure at which the first gas bubble appeared was recorded. The pressure in the instrument was measured with a precision spring manometer set on an oil press, and thereby a correction was made for the difference between the mercury level in the glass tube and that in the right-hand cylinder of the buffer.

A great advantage of the method described for investigating supersaturated gas-fluid solutions is that every measurement may be repeated many times without disassembling the apparatus. Usually, the experiment was repeated 5-8 times, and the average, P, was calculated.

Then the instrument was disassembled, again filled with the same fluid and the same gas but in a different proportion, and a new study was made.

Experimental Data

Results of the investigation are shown in the Table and in Figure 2.

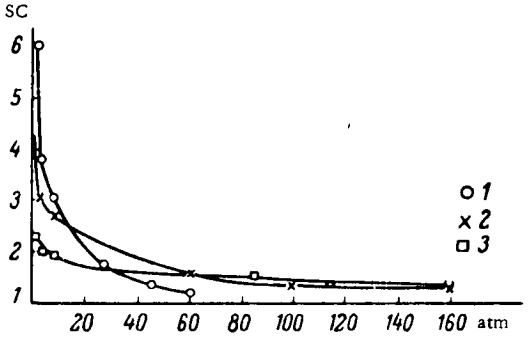


FIGURE 2. The SC of gas-fluid solutions as a function of the tension of the dissolved gas at 25°

On the abscissa, the pressure difference (in atmospheres); on the ordinate, the supersaturation coefficient. 1. CO_2-H_2O; 2. N_2-H_2O; 3. He-H_2O.

The results obtained show that the SC of all solutions decrease with increase of the tension of the dissolved gas P_0, i.e., with increase in its concentration. This change in SP is more pronounced in solutions of gases which dissolve readily in water. Thus, with a tension of the dissolved gas equal to 1 atm, the solutions investigated are arranged in

the following order with respect to the value of the SC:

$$CO_2 - H_2O - 6.06,$$

$$N_2 - H_2O - 4.04,$$

$$He - H_2O - 2.26.$$

With increase of the tension of the dissolved gas to 60 atm in a solution of the readily soluble gas, CO_2 (solubility coefficient $\lambda = 0.759$ ml/ml),, the SC decreases to 1.29 and becomes less than in solutions of poorly soluble gases — nitrogen ($\lambda = 0.0512$ ml/ml) and helium ($\lambda = 0.0099$ ml/ml) — in which the SC's are equal and about 1.50.

Supersaturation coefficients of gas-fluid solutions at different pressures (at 25°)

Solvents	Gas	P_0 (in atm)	P (in atm)	SC	$P_0 - P$ (in atm)
Water	Helium	0.97	0.43	2.26	0.54
		4.0	2.1	1.90	1.9
		8.0	4.5	1.78	3.5
		84	55	1.53	29.0
		114	80	1.42	34.0
		160	119	1.34	41.0
Water	Nitrogen	0.97	0.24	4.04	0.73
		4.0	1.28	3.12	2.72
		8.0	2.93	2.73	5.07
		60	39.5	1.52	20.5
		99	72	1.37	27.0
		160	120	1.33	40.0
Water	Carbon dioxide	0.97	0.16	6.06	0.81
		4.0	1.07	3.74	2.93
		8.0	2.73	2.93	5.27
		26	16.5	1.57	9.5
		45	32.5	1.38	12.5
		60	46.5	1.29	13.5
Benzene	Helium	0.86	0.15	5.73	0.71
		4.0	0.91	4.39	3.09
		8.0	2.4	3.33	5.60
Benzene	Nitrogen	4.0	0.75	5.33	3.25
		8.0	2.5	3.20	5.5
Benzene	Carbon dioxide	4.0	0.46	8.69	3.54
		8.0	1.75	4.57	6.25

The rules and regulations established may be explained by existing data on the study of high-pressure gas-fluid solutions. It has been proved experimentally (Shiller, 1897; Pollitzer and Strebel, 1924; Sage and Lacey, 1936; Brestkin, 1947) that with increase in the pressure at which the fluid is saturated with gas, the density of saturated vapor increases, and the density of fluid decreases, i.e., a gradual approximation of the properties of the liquid phases occurs. At some very high pressure, as

a rule, a critical condition occurs in the solution at which the vapor and the liquid phases become identical: the surface tension of the fluid drops to zero, and the SC becomes equal to one. The higher the gas pressure, the lower the critical temperature of the fluid. There is reason to believe (Ipat'ev, Teodorovich, Brestkin, Artemovich, 1948) that even at 37° the water may be brought up to a critical state, dissolving gas in it at a pressure of several thousand atm.

Therefore, with increase in the tension of the dissolved gas, the SC of the "gas-fluid" solutions at the given temperature should gradually decrease until a critical state occurs at some very high pressure at which supersaturated solutions cannot exist, and the supersaturation coefficient becomes equal to one. It is well known (Rysakov and Brestkin, 1937) that at the same temperature the critical state in the "gas-fluid" solution with a readily soluble gas is reached at a lower pressure than with a poorly soluble gas. Therefore, despite the fact that at low pressures the supersaturation coefficient is higher in "readily soluble gas-fluid" solutions than in "poorly soluble gas-fluid" solutions the limiting value of the supersaturation coefficient (1) in the first case is reached at a lower pressure than in the second. Therefore, on the coordinates of "supersaturation coefficient plotted against pressure" the curve for "readily soluble gas-fluid" solutions should intersect the curve for "poorly soluble gas-fluid" solutions (Figure 2).

In contrast to the SC, the difference $P_0 - P$ does not decrease but increases markedly with increase in the tension of the dissolved gas. For example, at a tension of dissolved helium equal to 0.97 atm, it is equal to 0.54 atm; at $P_0 = 160$ atm it increases to 41 atm. Because at the critical point $P_0 - P$ is evidently equal to 0, at very high pressure the value of this difference should, after reaching a maximum, decrease with further increase in pressure.

The data of the table shows graphically that with increased tension of the dissolved gas the value of SC is more stable. This fact has not been given a strict theoretical substantiation. In its most general form it may be explained on the basis of the Laplace equation,

$$P' - P = \frac{2\sigma}{r},$$

where P' is the pressure inside the gas bubble,
σ is the surface tension coefficient;
r is the radius of the bubble.

Let us take $P' = P_0$, then

$$P_0 - P = \frac{2\sigma}{r}, \tag{1}$$

from which

$$\frac{P_0}{P} = \frac{2\sigma}{Pr} + 1 \tag{2}$$

From equation (1) it follows that the difference $P_0 - P$ may remain constant with increase in P_0, if the ratio $\frac{\sigma}{r}$ does not change. As stated above, with increase in the concentration of the dissolved gas, σ decreases even when P_0 is very high; when the gas-fluid system reaches the critical state, σ becomes equal to 0. Since in our case P_0's are relatively low, the change in σ may be neglected. However, the change in r cannot be neglected; with increase in P_0 it should decrease.

Let us suppose that at a temperature of 25°, P_0 equals 2 atm in 1 ml of N_2 - H_2O solution. Let us suppose further that the first gas bubble in this solution was formed when the pressure was reduced to 1 atm. If σ of the solution = σ of water = 72 dynes/cm, $r = \frac{2\sigma}{P_0 - P}$ equals 1.42 μ, and the volume of the bubble $V = {}^4/_3 \pi r^3 = 11.9\ \mu^3$. In this bubble there will be about $5 \cdot 10^7$ molecules, whereas the entire excess of dissolved N_2 formed in 1 ml of solution with reduction of the pressure from 2 to 1 atm will be 0.0152 ml (solubility coefficient) or $4 \cdot 10^{17}$ molecules.

Let us now take $P_0 = 10$ atm. If the difference $P_0 - P$ remained constant, the first gas bubble would be formed at $P = 9$ atm. The radius and volume of the bubble would thereby be maintained. The excess of dissolved N_2 in 1 ml of supersaturated solution would also remain $4 \cdot 10^{17}$ molecules. However, the number of molecules in the bubble formed will not be $5 \cdot 10^7$, but 5 times more, $25 \cdot 10^7$.

Therefore, if the difference $P_0 - P$ did not change with increase in P_0, the probability that $5 \cdot 10^7$ molecules of N_2 will go into the bubble from 1 ml of solution containing an excess of $4 \cdot 10^{17}$ molecules would be the same as the probability that $25 \cdot 10^7$ N_2 molecules will go into the bubble from 1 ml of solution containing the same $4 \cdot 10^{17}$ molecules in excess, which is impossible.

From the calculation presented it follows that with increase in P_0 the radius of the bubble should decrease markedly, and the difference $P_0 - P$, necessary for the formation of the bubble should increase, which is in agreement with the experimental data obtained. According to equation (2), the ratio P_0 / P changes less, as a result of the fact that with increase in P_0 the reduction of r is compensated for by the increase occurring in P. At the critical point of the solution, at which $\sigma = 0$, in accordance with equations (1) and (2) the difference $P_0 - P = 0$, and the ratio P_0 / P equals 1.

Conclusions

At a temperature of 25° we determined the supersaturation coefficients of solutions of He- H_2O and N_2- H_2O in the pressure range from 1 to 160 atm; for the CO_2- H_2O solution, in the pressure range from 1 to 60 atm; in He- C_6H_6, N_2- C_6H_6, and CO_2- C_6H_6, in the pressure range from 1 to 8 atm. As a result of the investigation made, the following was determined.

1. With increase in the tension of the dissolved gas, SC decreases gradually in all solutions.

2. The reduction of SC with increase in the tension of the dissolved gas is observed to a greater degree in solutions of a gas readily soluble in fluid than in solutions of a gas poorly soluble in fluid.

3. In all cases, with increase in P_0 the ratio P_0/P is more stable than the difference $P_0 - P$.

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STUDY OF THE SAFE SUPERSATURATION OF THE BODY WITH INDIFFERENT GASES AT DIFFERENT PRESSURES

(Issledovanie bezopasnogo peresyshcheniya organizma indifferentnymi gazami pri razlichnykh davleniyakh)

In studying the mechanism of development and particularly of prevention of decompression disorders, it is very important to determine the degree of supersaturation of the animal or human body with indifferent gases at which the first symptoms of these disorders occur. In the experimental determination of the value of this supersaturation and in its quantitative characterization, it is essential to consider a number of circumstances associated with the specific properties of the supersaturated gas-fluid solutions themselves and with the body's reactions to gas bubbles formed in the tissues and particularly in the blood.

Characterization of Different Cases of Supersaturation of the Body with Indifferent Gases

A solution in which the tension of the dissolved gas P_0 is greater than the ambient pressure P is called a supersaturated gas-fluid solution. Therefore, the degree of supersaturation of such a solution may be characterized either by the ratio P_0/P, by the difference P_0-P, or simply by the value P_0, keeping P strictly constant, e.g., equal to 1 atm. Supersaturated gas-fluid solutions like all other supersaturated solutions are metastable systems and from a strictly theoretical viewpoint, stable gas bubbles can be formed in them at any degree of saturation if the condition $P_0>P'>P$ is fulfilled, where P' is the pressure in the gas bubble (Brestkin, 1958). In those cases where, as a result of fluctuation in the supersaturated solution, a gas bubble with an exceeding small radius is formed with a surface tension coefficient of σ, it is unstable and disappears quickly, because, according to the Laplace formula $P'-P=\frac{2\sigma}{r}$, the pressure in it reaches a high figure, exceeding P_0.

It has been proved (Volmer and Weber, 1926; Becker and During, 1935) that the probability of formation of stable gas bubbles in the supersaturated solution is greater with increased degrees of supersaturation. Because of the purely probabilistic nature of gas formation induced by random accumulation of numerous free gas molecules at any point in the supersaturated solution, the value of the characteristic supersaturation at which

the first stable gas bubble is formed in a certain period of time is not constant, even with strictest observance of conditions for preparation and subsequent observation of this solution. Therefore, in the experimental determination of this supersaturation value, great difficulties arise. As is well known, its value is determined by means of a successive increase in the degree of supersaturation by the same magnitude until a gas bubble appears in the given solution in a certain period of time.

Supersaturation is increased by two means: either by increasing the tension of the dissolved gas P_0 at a given ambient pressure P or by reducing P and keeping P_0 constant. Let us consider the first method.

Suppose no gas bubble formation is observed in a 20 minute period in a supersaturated solution of water-helium with $P_0 = 2.4$ atm where the ambient pressure is $P = 1$ atm, while gas bubbles are formed in a water-helium solution with $P_0 = 2.6$ atm under the same conditions ($P = 1$ atm and $t = 20$ min). Evidently, the degree of supersaturation P_{0z} sought in the helium-water solution is between the figures found empirically, 2.4-2.6 atm.

The concept of "maximum supersaturation," at which no gas-bubble formation is observed in the supersaturated solution and the concept of "minimum supersaturation," at which gas-bubble formation does occur is the same as the concept P_{0z}, just as two variables approaching a common limit from above and below coincide at the limit.

The exact value of P_{0z} may be found in the study of solutions with different P_{0z}'s within the 2.4 and 2.6 atm range and differing from one another by an infinitely small figure. However, this means accurate determination of P_{0z} is impossible because of its characteristic inconstancy. If, incidentally, we consider variations in the experimental measurements, it becomes clear that even for the simplest supersaturated solutions consisting of one gas and a pure fluid we can speak only of some average values for the supersaturation, P_0, which must be calculated from quite a large number of observations.

Quantitatively, the supersaturation corresponding to P_{0x} is characterized either by the supersaturation coefficient SC = P_0/P or by the degree of supersaturation SC = $P_0 - P$, or simply P_0 with P given.

In accordance with the above, the supersaturation coefficient SC should mean either the maximum ratio of the tension of the dissolved gas P_0 to the pressure in the solution P, at which no gas bubble formation occurs in a given period of time, or, what is the same thing, the minimum ratio of the tension of the dissolved gas P_0 to the pressure in the solution P at which the first gas bubbles are formed in a given period of time. The degree of supersaturation $P_0 - P$ should be determined in a similar way.

When dealing with the supersaturation coefficients of the body tissues with indifferent gases, the conditions under which they have been determined should always be considered. Thus, in the experiments of A. P. Brestkin (1958) rabbits were killed in a pressure chamber after being under pressure for 4 hrs. After reduction of the pressure to normal, an observation was made of gas-bubble formation in various tissues of the dead bodies, and the values of SC were found for synovial fluid, blood, bone marrow, and fat. The data of these experiments differs substantially from the results of short-term experiments in which, following decompression, gas formation in the blood and other tissues of the animal is

observed intra vitam. In the former case the tissues are in an inactive state, and should be regarded as physicochemical media in which, at certain degrees of supersaturation, gas bubble formation occurs (physical SC). In the latter case an investigation is made of the capacity of the tissues for retaining the dissolved indifferent gas in a state of supersaturation during the course of their activity (physiological SC). It has been proved (Harvey, 1944, 1945, and 1951) that the blood pulsation and muscle contractions considerably facilitate gas bubble formation in the body.

Supersaturation at which the first signs of decompression sickness occur in man and animals is of particular interest. As is well known (Pirogov, 1852; Pashutin, 1881; Brestkin, 1954; Vavilov and Gramenitskii, 1958), the body can eliminate a considerable quantity of free indifferent gas without appreciable critical functional disorders. Therefore, the value of this supersaturation, of prime importance in the study of the development and prevention of decompression disorders, characterizes not only the capacity of the tissues for retaining the dissolved indifferent gas in a supersaturated state, but also the compensatory reactions of the body directed at eliminating free gas.

This dangerous but still permissible supersaturation is quantitatively expressed in three ways: either by the ratio P_0/P, called the permissible supersaturation coefficient (PSC), or by the difference P_0-P, called the permissible supersaturation value [velichina], or simply by the figure P_0 with an ambient pressure of 1 atm, which, at the suggestion of I. I. Savichev, is called the limit. If the ambient pressure is not equal to 1 atm, the limit is calculated from the formula $P_0-(P-1)=P_0-P+1$, where $P-1$ is the manometric or excess pressure, i. e., the pressure measured with a manometer.

Of these three possibilities, the PSC method is best. This conclusion was drawn also by Haldane (1908), who, in experiments with goats, found that with increase in the tension of the dissolved indifferent gas, the ratio of pressures is more stable than the difference.

It should be noted that the Haldane coefficient (HC) is the ratio of the tension of the dissolved gas (usually nitrogen), P_0, in the body tissues to the partial pressure of this gas in the inhaled air, P_{N_2} after decompression. HC is related to the PSC by the following formula: $\text{PSC} = \text{HC}\,\frac{80}{100} = 0.8\ \text{HC}$, where 80 is the percentage of nitrogen in the inhaled air.

Haldane's method of expressing supersaturation cannot be considered correct: it is at variance with physicochemical concepts of supersaturated solutions and leads to confusion in the calculations when artificial breathing mixtures are used (Brestkin, 1952). When a person begins to breathe pure oxygen at normal pressure, the ratio P_0/P_{N_2} reaches a much higher figure than when a diver rises rapidly from great depths. Whereas in the first case, there is no nitrogen supersaturation of the body, $P_0-P=0.8-1<0$, in the second case the nitrogen supersaturation reaches an exceedingly high figure: $P_0-P>0$. At present the Haldane coefficient is not used, but his conclusions about the relative constant of the pressure ratio with increase in P_0 continues, in our opinion, to be valid.

Experimental determination of the PSC in man and animals present much greater difficulties than the determination of the SC for solutions of gas in the pure fluid. Here, aside from variations in supersaturation at

which gas bubble formation begins, the variability of the body's reaction to gas formation, which is of incomparably greater importance, must also be considered. Even with strictest observance of conditions, identical body reactions of the animals directed at elimination of the gas bubbles formed cannot be assured. This is evidenced in the work by V. A. Aver'yanov, P. M. Gramenitskii and A. A. Savich (1961), which shows that with systematic repetition of the experiments for determining the PSC in dogs, its value increases sharply, i. e., a distinctive training of the organism is observed. Only when the body's reaction to the gas bubbles formed becomes constant does the value of the PSC in the trained animal become more or less constant also.

Naturally, there is a certain amount of risk in using the experimentally determined PSC to calculate decompression conditions. Therefore, a considerably smaller figure is used, called either the calculated PSC or, more frequently, the safe supersaturation coefficient (SSC). From what has been stated it follows that the term PSC is substantially different from the term SSC. The permissible supersaturation coefficient (PSC) is the ratio of the tension of an indifferent gas P_0 dissolved in the body tissues to the outside pressure P, at which the first mild symptoms of decompression sickness occur in man or animal. The safe supersaturation coefficient (SSC) represents the ratio of the tension of the gas P_0 dissolved in the body tissues to the outside pressure P, at which it is known that no symptoms of decompression sickness occur, even the mildest.

In calculating decompression conditions of divers coming up from great depths the SSC is used, which is two thirds or even half of the PSC. However, even when the divers come up according to calculated conditions severe forms of caisson disease frequently occur. Because of this, some specialists (Behnke, 1937; Savichev and Bukharin, 1957) believe that the deeper the divers descend, i. e., with increase in P_0, the ratio P_0 / P decreases sharply, while the difference $P_0 - P$ remains relatively constant. To prove this, I. I. Savichev and A. N. Bukharin performed experiments on two guinea pigs, in which the characteristic limit was first determined for each animal, i. e., the maximum value of P_0 which, at an ambient pressure of 1 atm, does not yet cause decompression symptoms, and then experiments were performed with the so- called double limit. The animals were saturated with nitrogen for 6 hrs, at a partial pressure twice the limit, after which the depth was changed to correspond to the limit; this was maintained for another 6 hrs, and then a change was made to surface pressure. No decompression disorders in the guinea pig were noted by the authors. In two other experiments, where the depth of the first stop was determined on the basis of the coefficient, i. e., by the amount it was permissible to reduce the pressure, the authors recorded pronounced decompression disorders in the animals. Hence, they concluded that the measure of permissible supersaturation of the body with nitrogen is the difference between the tension of this gas and the manometric pressure, rather than the ratio P_0 / P. This data is in no way adequate for solving the principle problem of the main conditions determining gas formation which leads to development of functional disorders in the body during decompression. In connection with this, we performed the experiments presented below.

Method

The experiments were performed on five dogs and six cats. We first determined for each animal the maximum tension of dissolved nitrogen (P_0) at which under normal pressure conditions (P_n) no decompression disorders occur. For this purpose, the animals were kept for 4 or 6 hrs under pressures of 2.2 atm or higher with subsequent rapid decompression to normal pressure. The pressure in each subsequent experiment was increased by 0.2 atm until symptoms of decompression disorders developed in the animal. The nitrogen tension P_0 recorded in previous experiments, in which no decompression symptoms were noted, was taken as the measure of resistance of the given animal to decompression disorders. This value P_0, according to the concepts of I. I. Savichev and A. N. Bukharin, characterizes the limit for the animal; under the given conditions it represents the safe supersaturation coefficient of the body, SSC = $P_0 / P_n = P_0 / 1 = P_0$. In the case of decompression from high pressures but to some other pressure than normal, the values for the limit and the SSC diverge markedly. In accordance with the above, we took a value for the SSC not much different from the PSC.

After the determination of the P_0 value for each of the experimental animals, the basic experiments were performed. The animals were placed under a pressure of P_1 for 4 or 6 hrs, or one from which they might be taken out with a single 4 or 6 hour stop at a pressure of P, keeping constant SSC = P_0 established for this animal, both in the cases of decompression before the stop and with subsequent decompression to normal pressure P_n. In other words, P and P_1 satisfied the following conditions:

$$\frac{P_1 \cdot 0.8}{P} = \frac{P_{0.1}}{P} = \text{SSC} = P_0, \tag{1}$$

$$\frac{P \cdot 0.8}{P_n} = \frac{P_0}{1} = \text{SSC} = P_0 \tag{2}$$

From condition (2) we have $P = P_0/0.8$. By substituting the value of P found into condition (1), we determine the value of P_1:

$$\frac{P_1 \cdot 0.8}{\frac{P_0}{0.8}} = P_0, \text{ from which } P_1 = \frac{P_0^2}{(0.8)^2} = \frac{P_0^2}{0.64}$$

In a number of experiments, the values of P_1 and P were calculated from figures less than P_0, since according to existing data (Boycott, Damant, and Haldane, 1908; Brestkin, 1952; Zal'tsman and Zinov'eva, 1963), the SSC decreases with increase in the tension of the dissolved indifferent gas.

The dogs and cats were observed continuously during the experiments, and a careful record was made of every occurrence of decompression disorders, both after the first stop and after final decompression at the surface. Unquestionable signs of decompression disorders in dogs were of the "bends" type in the limbs; in cats, either the same symptoms or marked change in the general condition — loss of coordination of movements, severe general inhibition and intense dyspnea.

TABLE 1

Results of experiments on dogs with descent to great depths

Date of experiment (1959)	Depth corresponding to the permissible supersaturation value of the animals (in m)	Coefficient or limit (P_0)	Depth (in m) and exposure time (in hrs)	SSC used in experiment	Depth of the actual stop according to the SSC (in m)	Value of the limit in the first stop	Depth of the first stop according to the established limit (in m)	Signs of decompression disorders	
								At the first stop	After decompression at the surface
1	2	3	4	5	6	7	8	9	10
				The dog Mishka					
2 XI	12	1,76	57,5-4	1,92	18	3,60	36,4	Present	
9 XI	12	1,76	38,0-4	1,74	12	2,64	20,8	Absent	Absent
16 XI	12	1,76	57,5-4	1,74	21	3,30	36,4	Absent	Gradual decomposition
23 XI	14	1,92	47,0-4	1,90	14	3,16	26,4	Absent	Present
17 XII	16	2,08	57,5-4	2,08	16	3,80	33,2	Absent	Present
				The dog Sedoi					
13 XI	12	1,76	38,0-4	1,74	12	2,64	20,8	Absent	Absent
26 XI	14	1,92	47,0-4	1,9	14	3,16	24,6	Absent	Absent
2 XII	16	2,08	57,0-4	2,06	16	3,76	32,8	Absent	Absent
				The dog Rezhik					
18 XI	16	2,08	57,5-4	2,08	16	3,80	33,2	Absent	Present
24 XI	16	2,08	38,0-4	1,74	12	2,64	17,6	Absent	Absent
				The dog Bogatyr'					
19 XI	18	2,24	68,0-4	2,22	16	4,64	40,0	Present	—
27 XI	18	2,24	47,0-4	1,9	14	3,16	23,2	Absent	Absent
8 XII	18	2,24	57,5-4	2,08	16	3,80	31,6	Absent	Absent
				The dog Reks					
1 XII	20	2,40	57,5-4	2,08	16	3,80	30,0	Absent	Present

Results of the Investigation

The data of experiments on dogs is given in Table 1. Column 2 of the table ("depth corresponding to the permissible supersaturation value of the animals ") shows the maximum depths* at which, after 2 hours, there were no decompression disorders in the animals at normal pressure; column 3 , the nitrogen tension in the body, P_0 (defined either as the limit or as the safe supersaturation coefficient, SSC) is shown corresponding to these depths. Repeated determinations of this value were made during the course of these experiments; in agreement with the data of V. A. Aver'yanov, P. M. Gramenitskii, and A. A. Savich (1961), an increase in resistance to decompression disorders was noted in some dogs, i. e., there was an increase in the SSC. Columns 4 and 6 give the depths corresponding to pressures P_1 and P, and column 5 shows the values of the PSC from which the P_1 and P values were calculated. In column 7 the limit figures are given in the case of decompression from the initial depth to a certain stop — $P_{0,1}-P-1$. Column 8 indicates the depths of the first stops which must be used in experiments on the basis of the constancy of the limit, $P_{0,1}-P_0=P_x$, where Px is the manometric pressure at the stop; when we multiply P_x by 10 we obtain the depth corresponding to the manometric pressure in meters of water. The data of the other columns are not needed in the explanations.

The results of the observations presented in Table 1 show that at the first stop decompression disorders occurred in only two experiments; in one case (experiment on 2 November) the coefficient used in the calculation was higher than the PSC. After ascent to the surface decompression disorders occurred in 4 out of 11 cases; the other seven experiments did not show these disorders.

The results of the experiments on cats are shown in Table 2. In this series of experiments, as a rule, the figures used for the PSC were usually less than those established in preliminary investigations. Two experiments were exceptions: in one (on 1 June) the coefficient did not increase; in the other (on 11 November) it increased. Both these experiments ended in the death of the animals at the first stop. Of the remaining 13 experiments, decompression disorders at the first stop occurred in only two cases. Here the actual depths of the first stops differed from those calculated from the limit by an even greater extent than in experiments on dogs, despite the fact that the limit used was equal to P_0 (column "coefficient or limit P_0") without reduction of this value.

In only one of 11 completed experiments did decompression disorders occur in an animal after final decompression. In the other 10 experiments both degrees of decompression occurred without signs of decompression disorders.

The results of these experiments show that the safe supersaturation coefficient cannot be considered the same for different conditions: it decreases with increase in the absolute pressure at which the body is saturated with the indifferent gas. It is not yet possible to say definitely whether this change in coefficient is based chiefly on physicochemical rules and regulations, or whether a change in the body functions occurs

* The accuracy of determination of these depths was within 2 m of water or 0.2 atm.

TABLE 2

Results of experiments on cats with descent to great depths

Date of experiment	Depth corresponding to the permissible supersaturation value of the animals (in m)	Coefficient or limit (P_0)	Depth (in m) and exposure time (in hrs)	SSC used in experiment	Depth of the actual stop according to the SSC (in m)	Value of the limit in the first stop	Depth of the first stop according to the established limit (in m)	Signs of decompression disorders	
								At the first stop	After decompression at the surface
1	2	3	4	5	6	7	8	9	10
				Cat No. 1					
1 VI	22	2.56	90.0-4	2.50	22	5.8	54.4	Death from caisson disease	—
				Cat No. 2					
21 VII	28	3.04	90.0-6	2.35	24	5.6	49.6	Absent	Absent
2 X	28	3.04	90.0-6	2.5	22	5.3	49.6	Absent	Absent
1 XI	28	3.04	85.0-6	2.37	22	5.4	45.6	Absent	Absent
11 XI	28	3.04	10.5-4	2.7	24	6.8	61.6	Absent	Absent
19 XI	28	3.04	120-4	2.89	26	7.8	73.6	Absent	Present
				Cat No. 3					
25 XI	28	3.04	90-6	2.2	26	5.4	49.6	Present	—
				Cat No. 4					
28 IX	24	2.72	75-6	2.27	20	4.8	40.8	Absent	Absent
9 X	24	2.72	75-5	2.27	20	4.8	40.8	Absent	Absent
10 IX	24	2.72	92-4	2.56	22	6.0	54.8	Present	—
20 XI	24	2.72	92-4	2.56	22	6.0	54.8	Absent	Absent
				Cat No. 5					
11 XI	22	2.56	75-4	2.8	14	5.4	42.4	Death from caisson disease	—
				Cat No. 6					
9 XI	26	2.88	75-4	2.27	20	4.8	39.2	Absent	Absent
16 X	26	2.88	92.5-4	2.56	22	6.0	53.2	Absent	Absent
26 XI	26	2.88	92.5-4	2.56	22	6.0	53.2	Absent	Absent

which is associated with the action of depth factors. As far as the limit is concerned, we cannot speak of its constancy. With increase in the tension of the indifferent gas it increases markedly. As the data of Table 2 show, when the animals rise from depths of 80—100 m, the established figure for the PSC should be reduced 20—25%, while value of the limit should be increased 1.5—2 times.

The data obtained shows objectively that the use of a constant value for the limit in the case of decompression from high pressures entails an increase in the depths of the first stops, which necessitates a substantial increase in decompression time. Thus, if cat No. 2 was raised from a depth of 105 m (experiment of 11 November, Table 2), using constancy of the limit as a guide, two 4 hour stops should be made rather than one — the first at a depth of 61.6 m and the second at a depth of 27 m. All this indicates that the notion of limit constancy is incorrect, and its application is not reasonable for calculations of decompression conditions.

Conclusions

1. It is better to determine the limiting supersaturation of the body tissues with an indifferent gas by the ratio of the gas tension to the ambient pressure after decompression than by the difference between these figures.
2. The notion of constancy of the limit is incorrect: with increase in the tension of the dissolved indifferent gas, the value of the limit increases sharply.
3. With increase in the tension of the dissolved indifferent gas the value of the safe supersaturation coefficient (SSC) decreases, which agrees with the data of other authors.

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G. L. Zal'tsman and I. D. Zinov'eva

COMPARATIVE DETERMINATIONS OF THE PERMISSIBLE SUPERSATURATION VALUE OF THE HUMAN BODY WITH INDIFFERENT GASES UNDER DIFFERENT CONDITIONS

(Sravnitel'noe opredelenie velichiny dopustimogo peresyshcheniya organizma cheloveka indifferentnymi gazami v raznykh usloviyakh)

The permissible supersaturation value of the body with an indifferent gas was first determined by Haldane (1906) in experiments on animals. Such determinations were made on human beings by A. N. Bukharin (1958), I. A. Aleksandrov and A. P. Brestkin (1964).

Method

The degree of permissible supersaturation has been determined in the following way. For 6 hrs (time needed for complete saturation of the body with the indifferent gas, in Haldane's opinion) the subjects were under increased pressure, after which rapid decompression was conducted (for 1—2 min). The pressure from one determination to the next increased 0.2 or 0.3 atm until the subjects developed the first signs of decompression disorders on leaving the chamber.

To simplify the method described, we worked out an accelerated method for the same determination. It has been shown (Zal'tsman, 1961) that for determining the permissible supersaturation value complete saturation of the body with an indifferent gas is not necessary, since the duration of this process is actually much longer than 6 hrs. Maintaining the same principle in the determination, the permissible supersaturation value may be established by keeping the subjects under pressure for much shorter periods (5—90 minutes) but under higher pressures.

It should be specially noted that in both the 6 hour and accelerated method, the appearance of the first subjective and objective signs of decompression sickness constitutes the indication of supersaturation. This has a substantial effect on the accuracy of the determinations. Greater accuracy therefore can be obtained by comparative determinations of the permissible supersaturation value made in the same subjects under different conditions.

In the present study the effects of such important conditions as breathing various gas mixtures and the action of various external pressures were

evaluated according to the data of a comparative determination of the permissible supersaturation value.

In the first series of investigations on three subjects (professional divers) a comparative determination was made of the permissible supersaturation value after the inhalation of air, 20% helium-oxygen mixture, a 50% air-helium mixture (50% helium, 39.6% nitrogen and 10.4% oxygen) and a 75% air-helium mixture (75% helium, 19.8% nitrogen and 5.2% oxygen)*. The subjects were placed in a dry compression chamber where they used a self-contained breathing apparatus (the cannisters of the apparatus were charged with substance 0-3). The composition of the inhaled gas mixture was checked periodically by gas analysis. The compression lasted 1—2 min. The time spent under increased pressure was exactly 1 hr, after which decompression for 2—2.5 min was conducted. In the first determination the pressure was increased to 3 atm, and in all subsequent determinations made after 2—3 days, it was increased by 0.25 atm, until the first signs of decompression sickness appeared after decompression. Therefore, the permissible supersaturation value was determined with an accuracy of 0.2—0.24 atm. Initially, the determinations of the permissible supersaturation value were made with the subjects breathing air, then helium-oxygen, air-helium mixtures, and again with air.

In the next series of investigations a comparative determination was made of the permissible supersaturation value in two subjects at different initial pressures. In order to determine how the permissible supersaturation value varies in accordance with the initial pressure level it was necessary to obtain at least three points for construction of the curve, that is, to determine the permissible supersaturation value for three different initial pressures in the same subjects. The pressure for safe surfacing served as the first point, normal atmospheric pressure with subsequent rarefaction as the second, and the greatest prenarcotic pressure of the air—7 atm was selected as the third. The maximum permissible pressure drop was then determined.

The method of determination was the following. By the 6 hour method a determination was made of the permissible supersaturation value for the maximum pressure, which may be rapidly reduced to normal without signs of decompression sickness.

The permissible supersaturation value for atmospheric pressure was determined in a vacuum pressure chamber. In the first determination the pressure was reduced to 0.405 atm (which corresponds to an altitude of 6000 m). The subjects remained under this pressure in an oxygen apparatus for an hour. In each successive determination the pressure was reduced 0.1 atm until the first signs of decompression sickness occurred in the subjects when held at a stop**. The duration of the first stop, as in the previous determinations, was 1 hr: as was determined previously, the symptoms of decompression sickness usually occur within a half-hour when the safe pressure drop is exceeded.

* The 75% air-helium mixture was enriched with oxygen so that its partial pressure "at ground level" was 0.2 atm.

** With the appearance of signs of decompression sickness the pressure was raised again to 7 atm. The subjects were kept at this pressure until the complete disappearance of signs of the disorder, after which decompression according to a specially calculated routine was used.

TABLE 1

Results of determination of the degree of permissible supersaturation on breathing various gas mixtures

Subjects	Air				20% helium-oxygen mixture				50% air-helium mixture				75% air-helium mixture			
	maximum safe pressure (in atm)	minimum safe pressure (in atm)	permissible supersaturation value		maximum safe pressure (in atm)	minimum safe pressure (in atm)	permissible supersaturation value		maximum safe pressure (in atm)	minimum safe pressure (in atm)	permissible supersaturation value		maximum safe pressure (in atm)	minimum safe pressure (in atm)	permissible supersaturation value	
			coefficient	difference			coefficient	difference			coefficient	difference			coefficient	difference
Ch-i	3,0	3,25	2,4	1,4	3,5	3,75	2,8	1,8	3,31 (3,75)	3,54 (4,0)	3,0	2,0	3,2 (3,75)	3,38 (4,0)	3,0	2,0
M-v	3,25	3,5	2,6	1,6	4,25	4,5	3,4	2,4	4,2 (4,75)	4,42 (5,0)	3,8	2,8	3,97 (4,75)	4,18 (5,0)	3,8	2,8
K-s	3,75	4,0	3,0	2,0	4,5	4,75	3,6	2,6	—	—	—	—	—	—	—	—

Note. The air pressures at which the partial pressure of nitrogen corresponds to the partial pressure of nitrogen and helium in the air-helium mixtures are presented in parentheses. The permissible supersaturation values are calculated for 100%-saturated tissues. The difference is between the partial pressure of nitrogen (or helium) and the manometric pressure after decompression.

Results of the Investigation

The results of the first series of investigations, given in Table 1, show that the maximum pressure which may be safely reduced to normal after an hour's exposure depends on the indifferent component of the breathing mixture. Thus, with the helium-oxygen mixture this pressure was 0.5—1.0 atm greater than when breathing air; with air-helium mixtures, 0.25—0.5 atm greater than with the helium-oxygen mixture. Significantly, the permissible supersaturation value of the nitrogen of the air was confirmed on a repeat determination. On the basis of the results of the determinations the coefficients and the differences characterizing the value of the safe supersaturation of the body with nitrogen, helium and their mixtures may be calculated (Table 1).

It should be noted that the nature of the symptoms of decompression sickness which occurred differed substantially with the various gas mixtures. Thus, on breathing air the first symptom was brief, painless itching of the skin. On breathing 20% helium-oxygen the only symptoms observed were deep muscle pains, after which it was usually necessary to perform therapeutic recompression. After breathing 50% air-helium, symptoms occurred which were usually "mixed" in nature; however, painful sensations were very slight, and sometimes did not occur at all. On breathing a 75% air-helium mixture the symptoms were usually of a "helium" character.

TABLE 2

Results of determination of the permissible supersaturation value of the body with the nitrogen of the air at different initial pressures (in atm)

Minimum dangerous pressure drop			Maximum safe pressure drop			Degree of permissible supersaturation	
initial pressure	partial nitrogen pressure	highest safe pressure for first stop	initial pressure	partial nitrogen pressure	highest safe pressure for first stop	increased nitrogen pressure (difference)	coefficient
1.0	0.8	0.405	1.0	0.8	0.465	0.335	1.72
2.3	1.84	1.0	2.2	1.76	1.0	0.76	1.76
7.0	5.6	4.2	7.0	5.6	4.3	1.3	1.3

Note. The permissible supersaturation value was calculated for tissues which were completely saturated with nitrogen during a 6 hour stay under pressure.

The results of the next series of determinations of the permissible supersaturation value were the same in both subjects (Table 2). As follows from the data of the table, the permissible supersaturation value changes substantially depending on the pressure at which the determination was made. The higher the initial pressure the greater the permissible supersaturation value. Thus, with increase in the pressure from 1.0 to 7.0 atm, it increases by 1 atm (from 0.3 to 1.3 atm). However, if the permissible

supersaturation value is expressed in the form of the nitrogen coefficient, with increase in the pressure the values of the coefficient decrease (Table 2).

The results obtained were checked on 17 subjects who underwent decompression favorably after a 4—6 hour stay under a pressure of 7.0 atm, with an hour's delay at the first stop under a pressure of 4.3 atm. At the last stop during decompression a brief itching of the skin was noted in only one subject. Therefore, a pressure drop from 7.0 to 4.3 atm was safe for 17 out of 18 [sic] subjects, despite the fact that the supersaturation value for a pressure of 7.0 atm exceeded the permissible supersaturation value determined in these subjects for an initial pressure of 2.2—2.9 atm. For a pressure of 7.0 atm it amounted to 1.3 atm; for a pressure of 2.2—2.7 atm, 0.76—1.2 atm, respectively.

This result was also checked in experiments on animals (5 cats). The permissible supersaturation values with the helium-oxygen medium at pressures of 4—5 and 31 atm were also compared after a 4 hour exposure. It was found that with an initial pressure of 4—5 atm the permissible supersaturation value was 2.2—3.0 atm, and at a pressure of 31 atm, 11.5 atm. Therefore, the permissible supersaturation value, determined by the pressure difference, increased 4—5 times (2.2—3.0 atm and 11.5 atm), while that calculated for the permissible supersaturation coefficient decreased by 50—62.5% (3.2—4.0 and 1.6).

Discussion of Results

It should be noted first that the safe permissible supersaturation coefficient of the organism should be interpreted as a physiological index. Since the SSC is determined by the signs of decompression sickness, it, in contrast to the simple physical systems, characterizes not only the capacity of the tissues for retaining gas in the supersaturated state, but also the body's reaction to a newly formed gas phase.

As shown by the studies made, the signs of decompression sickness differed substantially depending on the indifferent gas breathed. Similar results were obtained by I. A. Aleksandrov and A. P. Brestkin (1964) in subjects with a 6 hour determination method. The different reactions of the body to the formation of gas phases of different compositions are apparently an essential factor in determining the different permissible supersaturation values for nitrogen and helium. The data of P. M. Gramenitskii, A. A. Savich and K. S. Yurova (1964) confirms this, showing that the animals better tolerated an intravenous injection of nitrogen than one of helium. On the other hand, in Brestkin's experiments (1952) on simple physical models, opposite results were obtained; the supersaturation value of the fluids with helium was less than their supersaturation value with nitrogen. Therefore, physiological processes apparently play a major part in determining the safe permissible supersaturation of the body.

Like the indices of the other body functions, the permissible supersaturation value varies under different conditions, particularly as a function of the nature of the indifferent gas and the external pressure level.

Proper consideration of the actual values of the permissible supersaturation of the body with indifferent gases is necessary for safe decompression of divers.

The studies made showed that neither the principle of the constant difference nor of the constant coefficient can be used for calculating decompression routines. The calculations should be made by using the differential coefficient. There is no generally accepted method of differentiation. Values of the coefficient close to those determined experimentally are given by a method of differentiation in accordance with an empirical formula which we have used previously (Zal'tsman, 1961).

Conclusions

1. The safe supersaturation value of the human body depends on the characteristics of the indifferent gas: in a helium-oxygen medium this value increases by comparison with that in air; in an air-helium medium, it is over that in a helium-oxygen mixture.
2. The safe supersaturation value also depends on the external pressure level. The higher the initial external pressure, the greater the safe pressure drop.
3. The actual significance of the safe supersaturation value, determined under different conditions, should be considered in working out efficient decompression routines.

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V. A. Aver'yanov

SOME CONDITIONS FOR THE INCREASE IN BODY RESISTANCE TO DECOMPRESSION DISORDERS UNDER THE REPEATED EFFECTS OF DECOMPRESSION

(O nekotorykh usloviyakh povysheniya ustoichivosti organizma k dekompressionnym narusheniyam pri povtornykh vozdeistviyakh dekompressii)

In the study made by V. A. Aver'yanov, P. M. Gramenitskii and A. A. Savich (1961), the possibility was determined of increasing body resistance to decompression disorders under the influence of frequently repeated decompressions. In determining the safe supersaturation coefficient with nitrogen (SSC) for dogs, the authors kept the animals for 4—6 hrs under increased pressure (which in the initial experiments was known to be safe), and then subjected them to rapid decompression to the "surface level" and recorded the presence or absence of decompression disorders. Among the many determinations of the SSC previously made by this method, this work was distinguished by certain characteristics which enabled determination of an increase in body resistance to repeated decompression effects.

In previous investigations A. N. Bukharin (1958), G. M. Zarakovskii (1960), and other authors made their determinations only of the first case of decompression symptoms and after being convinced of the absence of these symptoms in the next experiment with lower pressure, they stopped the investigations, considering the SSC established. In the work by Aver'yanov, Gramenitskii and Savich, the experiments were continued, and in each successive experiment higher pressure was again used. The symptoms of decompression were usually absent. In the next determination the pressure was raised one step further (by 0.2 atm); if the symptoms occurred, it was again reduced in the next experiment, and then again increased. Thus, the studies were continued until the increased pressure was reached at which decompression disorders developed in the dogs every time, despite the frequent repetition of the experiments.

With this method, a considerable increase in resistance to decompression disorders was found in all nine dogs used in the work. At the end of the determinations these disorders occurred in each animal only after being under pressure 0.4—0.6 atm higher than at first.

The established fact that there is an increase in the resistance of the body to repeated decompression effects, which is of undoubted significance for diving practice, required further analysis. It remained unclear whether the conditions maintained in the work mentioned (gradual increase in pressure from one time to the next, and going to a lower pressure after

each case of decompression disorders) are obligatory and optimal for increasing body resistance to decompression. The question remained how resistance to decompression disorders would change under repeated effects of the pressure at which these symptoms originally occurred, as well as how it would change when the organism was first exposed to the action of a known high supraliminal pressure and subsequently, to the effect of progressively lower pressures. The solution of these problems is of practical as well as theoretical interest, because it can provide the basis of efficient work organization of divers, particularly novices.

Method

Ninety experiments were performed on seven male dogs from 3 to 5 years old, weighing 15—30 kg. The animals were put in a compression chamber under increased pressure for 4 hrs. At the end of this time the pressure was rapidly reduced to atmospheric, and the dogs were observed for 2 hrs. With the occurrence of decompression disorders (retraction of one of the paws, limping) therapeutic recompression was performed.

All the experiments were divided into two series. In the first series, performed on the dogs Ingus, Kashtan, and Matros, the experiments were begun with pressures known to be safe (1.4, 1.6, and 1.8 atm). In each subsequent experiment the pressure was increased by 0.2 atm until the dog developed compression disorders. Then the experiments were repeated with the same pressure.

In the second series (dogs Chernysh and Skuchnyi) the experiments were begun at a pressure of 2.8 atm, known to be safe; after the pressure effect was eliminated decompression disorders occurred in both experimental animals. Subsequently, the pressure was reduced from experiment to experiment until there were no symptoms of decompression disorders. Then the experiments were performed again with increasing pressures, and in various periods of the study it was left unchanged for a number of experiments,

Of the two variants of experiments described, those on the dogs Shustryi and Tobik, about which more details will be given below, stood out.

Results of the Experiments

The results of the experiments of the first series are given in Figure 1, which shows that in the dogs Ingus and Kashtan, exposed first to the effect of pressures known to be safe and then to gradually increasing pressures, decompression disorders occurred only at very high pressures, 2.8 and 3.2 atm. These figures are definitely higher than the average threshold pressures for dogs generally. Repeated experiments with both dogs at the pressures mentioned were associated every time with the development of decompression symptoms. Therefore, under these conditions the resistance did not increase further, and in the dog Kashtan it even decreased. The dog Matros originally showed symptoms of decompression

after being under comparatively low pressure (2.0 atm), but in repeated experiments these symptoms did not appear. However, after each successive increase in the pressure by 0.2 atm they did occur every time, either in the first or in subsequent experiments.

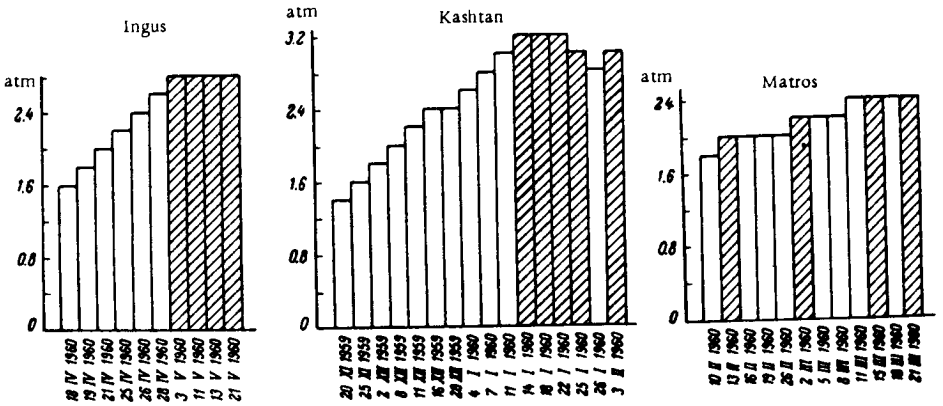


FIGURE 1. Change in the resistance to decompression sickness in the dogs Ingus, Kashtan, and Matros
white columns — no sickness; hatched colums — sickness.

Therefore, in this dog also, repetition of the experiments with the pressures at which the animals originally developed decompression symptoms did not lead to a considerable increase in resistance. This effect was undoubtedly less than in the above experiments of Aver'yanov, Gramenitskii, and Savich (1961).

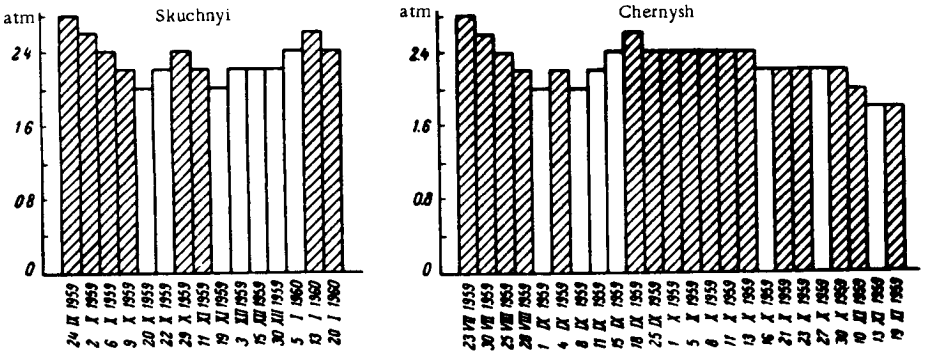


FIGURE 2. Change in the resistance to decompression sickness in the dogs Chernysh and Skuchnyi
Explanation in the text.

The results of the experiments of the second series are shown in Figure 2. Both dogs (Skuchnyi and Chernysh) were originally exposed to the action of a known safe pressure (2.8 atm). In both animals, in the

first and in the three subsequent experiments with gradually decreasing pressures decompression symptoms developed. These symptoms failed to appear only in the fifth experiment after decompression from a pressure of 2.0 atm, which is not the limit for the great majority of dogs. Therefore, with this course of the experiments not only do we fail to note an increase in the resistance of the animals to decompression disorders but, conversely, a decrease occurs. It is significant that with subsequent experiments, in which after the appearance of symptoms the pressure was dropped, the resistance temporarily increased in the dog Skuchnyi and in the dog Chernysh. Many repetitions of the experiments with the pressure at which decompression symptoms occur (the dog Chernysh) again led to a reduction in resistance, and the latter decreased even below the initial level.

A separate analysis should be made of the results of experiments on the dogs Tobik and Shustryi (Figure 3). With Tobik it had been planned to conduct the experiments along the line of the second series; therefore, at first a pressure of 2.8 atm was used. However, contrary to expectations, the animal did not develop decompression disorders, and it was therefore decided to increase the pressure gradually in the subsequent experiments. Such experiments showed the exceptionally high resistance of the animal to decompression disorders. The latter occurred first only after a pressure of 3.8 atm, which is about 1.5 atm higher than the average threshold value of the pressure for the majority of animals first exposed to the high pressure effect. We therefore began experiments on the dog Shustryi with a pressure of 3.2 atm and subsequently reduced it by 0.2 atm intervals, as in the other experiments of the second series. Decompression disorders in the dog occurred, however, only in the first two experiments; in the third, after a pressure of 2.8 atm they were absent. It was found, therefore, that this dog possessed increased resistance to decompression disorders, whereby, according to the general rule, following a drop to a lower pressure after the repeated development of symptoms, the resistance, very high before this, began to increase even further (Figure 3, experiments of 6, 9, and 12 July 1960).

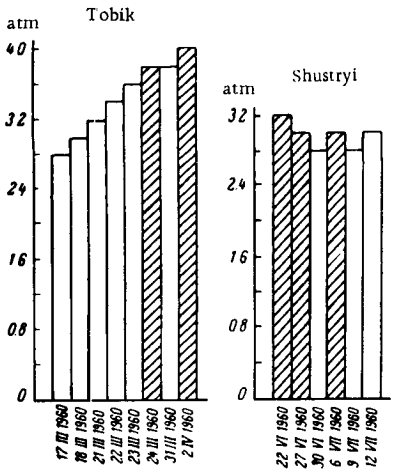


FIGURE 3. Change in resistance to decompression sickness in the dogs Shustryi and Tobik

explanation in the text.

Therefore, the results of the experiments just analyzed revealed the increased resistance of two experimental dogs to decompression disorders; at the same time, they do not at all contradict the data of the previous experiments.

Discussion of Results

The experiments performed showed that repeated decompression from pressures after which decompression disorders occur does not contribute to increasing body resistance to the given effect, and, conversely, it may even decrease. The initial use of pressures known to be high, far exceeding the threshold, has an even less favorable effect on the resistance of the body to decompression disorders. To increase resistance it is essential to increase gradually the pressure from initially low figures, known to be safe, to higher pressures; the best result is obtained from going to a lower pressure after each case of decompression disorders.

From the papers of Behnke and others (1940) and Evelyn (1941), confirmed recently by the studies of P. M. Gramenitskii and A. A. Savich (1964), it appears that after decompression "silent" gas bubbles may be formed in the body which do not lead to the development of visible pathological signs. These bubbles occur first in the venous blood and, according to the data of P. M. Gramenitskii and A. A. Savich, first appear after decompression from low pressures, beginning with 1.4 atm. It must be supposed that such bubbles in the venous blood can produce local vascular reflexes at the place where they occur, general changes in the cardiovascular activity, and a change in respiration because of a capillary block in the lesser circulation. The perfection of these reactions, expressed in an increased blood flow and dyspnea, apparently underlies the increase in body resistance to decompression disorders under repeated effects of decompression. An increase in resistance occurs only if there is an unusual stimulus to which the body adapts itself (free gas bubbles in the blood). At the time of the initial effects it proves inadequate to produce typical pathological symptoms, but subsequently, while still subliminal for the development of these symptoms, it increases in strength from time to time, which leads to training of the respiratory and cardiovascular defense reactions.

Conclusions

1. Repeated effects of decompression from increased pressure fail to lead to an increase in body resistance to decompression disorders which may occur.
2. The optimum condition for increase in body resistance to decompression disorders is the initial application of a pressure known to be safe, a gradual increase in it with subsequent effects and a drop to a lower pressure after the development of decompression symptoms.

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N66-17132

P. M. Gramenitskii and A. A. Savich

PROVOCATION OF CAISSON DISEASE SIGNS IN ANIMALS EMERGING FROM INCREASED PRESSURE BY SUBSEQUENT ASCENT TO ALTITUDE

(Provokatsiya kessonnykh yavlenii u zhivotnykh vyshedshikh iz pod povyshennogo davleniya, putem posleduyushchego pod'ema ikh na vysotu)

The results of a recent study which we made (Gramenitskii and Savich, 1964), in agreement with previous data from the literature (Yakobson, 1950; Vavilov and Gramenitskii, 1958; Behnke, 1955), gave us the basis to suppose that gas bubble formation in the body after decompression under increased pressure can occur asymptomatically or, in any case, without typical external signs of decompression disorders. With the aim of provoking signs of caisson disease and detecting latent forms, we performed experiments in which at various periods after decompression of the animal from increased pressure, they were raised to altitude, i.e., exposed to the effect of a rarified atmosphere. Use was made of increased pressures which were not followed by typical decompression disorders, and degrees of rarefaction which in themselves could not cause decompression disorders.

Method

The experiments were performed on nine dogs whose permissible supersaturation coefficient with nitrogen (PSC) previously had been repeatedly determined. The procedure was as follows: The fasting dog was walked, and then placed for 4 hrs in a compression chamber under pressure. For each animal the pressure used was known to be less than that which caused decompression disorders in experiments with determination of the PSC. In various experiments it ranged from 1.2 to 2.6 atm. After 4 hours, the dogs were exposed to a rapid (50—80 sec) decompression to normal pressure, and they were observed continuously. Under ordinary conditions caisson symptoms did not occur. At certain periods after decompression (from 15 min to 1 hr and 45 min) the dogs were exposed to the effect of rarefaction in a vacuum chamber (elevation to an altitude of 4.5 km at a rate of 1 km every 30 sec). The experimenters were either in the chamber along with the dogs, or outside it, using an illuminator to observe the animals. With the development of typical decompression symptoms (limping, elevation of the paw), a descent to ground level was made immediately; in the absence of disorders the animals were kept at an

altitude of 4.5 km for 10 min. The experimenters recorded the change in behavior, the condition of the dog and, very carefully, the development of decompression symptoms; in a number of cases the photographic documentation was used.

Results of the Experiments

Following decompression prior to elevation to altitude, the animals in no case showed caisson symptoms of the "bends" type. In some experiments only a very slight general inhibition of the dog and a mild dyspnea occurred. Ascents induced the development of typical signs of caisson disease in 25 out of 57 experiments. All cases in which symptoms developed with rarefaction of the atmosphere may be distinctly divided into two categories.

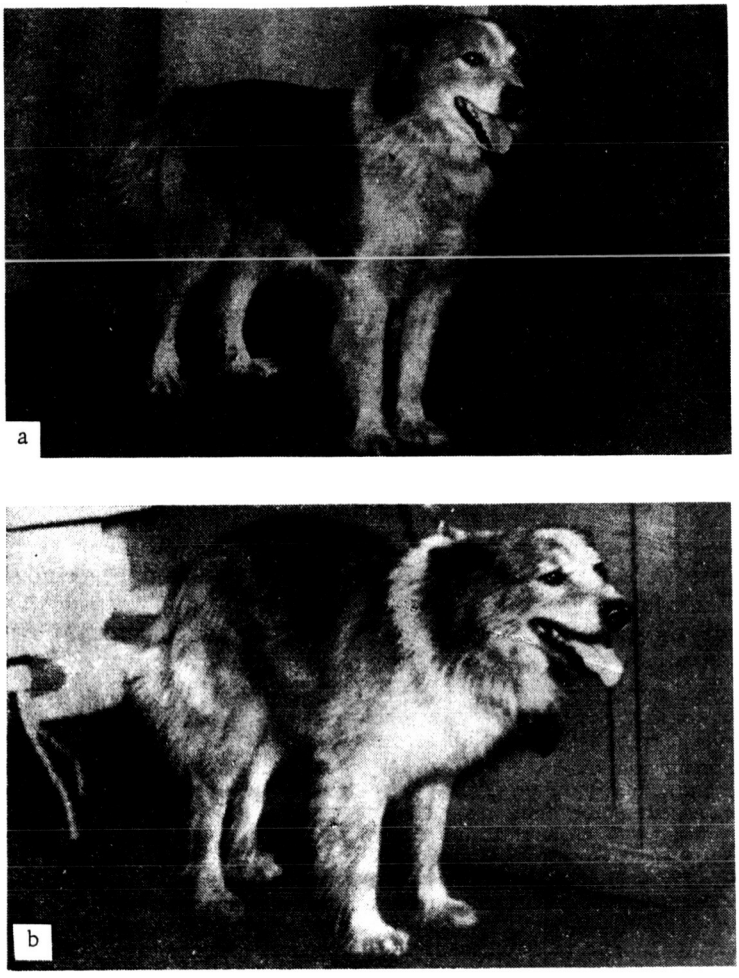
The first category consists of cases in which caisson disease symptoms developed at various periods after reaching the altitude. The actual ascent, i. e., the period of rarefaction of the air in the chamber, did not cause even initial signs of functional disorders of the limbs. At first, these signs were also completely absent at altitude. They appeared only after 2—5 min, gradually increased, and became clearly expressed caisson disorders. In all cases, the nature of the symptoms, and the dynamics and rate of their development were generally identical to decompression disorders under ordinary conditions after emerging from pressures exceeding the PSC for the dog.

The figures show gradual development of caisson symptoms at altitude in the dog Ryzhik.

The second category (of particular interest) consists of cases in which caisson symptoms developed during the course of the actual ascent. Not uncommonly, the first signs of decompression disorders appeared even from the very beginning of rarefaction of the air: the dog began to drag itself around in one place, reduce the weight on one limb or another, and "guarded" it. During the subsequent ascent, frequently to an altitude of 2—3 km, the symptoms became clearly expressed: the dog limped on the affected paw, became restless, tense, evidently had severe pain, and began to howl and jump about. In contrast to the decompression disorders described previously, events developed quickly and in full force: with continuing ascent the symptoms progressed literally with the rise in height and not uncommonly at an altitude of 4.5 km it reached such a degree that the ascent had to be stopped and the pressure increased in the chamber. With immediate descent and return of the animals to normal pressure, decompression symptoms always disappeared without trace.

The results of all 57 experiments are shown in the table.

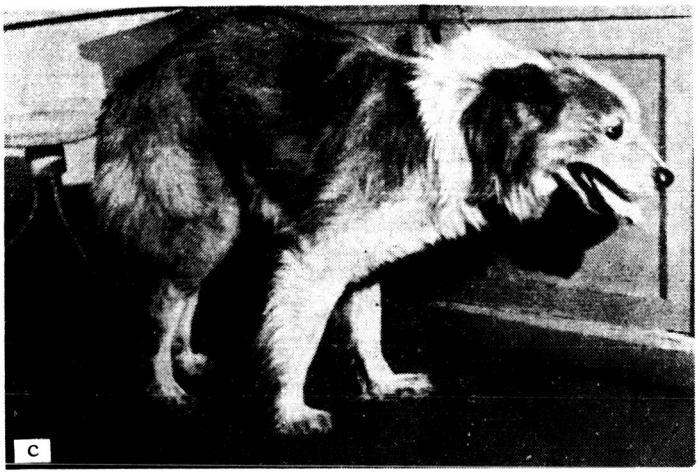
Gradual development of caisson symptoms after reaching an altitude occurred in 13 cases; rapid development of decompression disorders during the course of the ascent, in 12. From the table it is evident that both categories of disorders were noted in six animals after they had been at different depths, and at different intervals between decompression and ascent. The disorders appeared independently of the depth at which the animal was first. It should be emphasized only that caisson symptoms

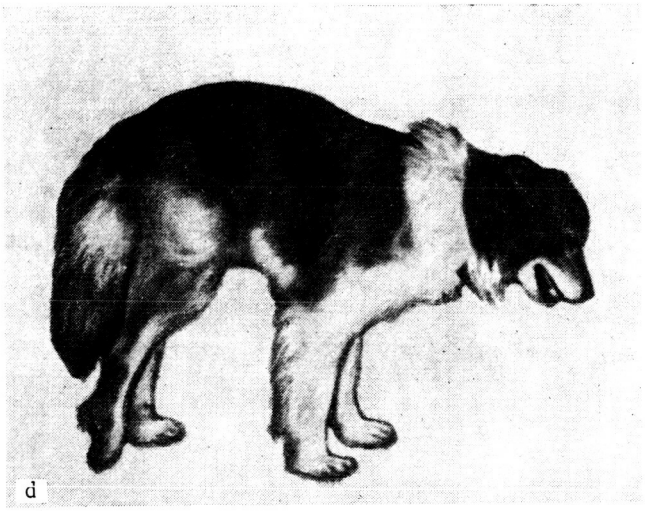


Provocation of decompression symptoms in the dog Ryzhik by means of ascent to an altitude after coming out of increased pressure

a — 13 min after decompression from a pressure of 1.6 atm, no signs of decompression disorders whatsoever; b — 2 min after ascent to altitude of 4.5 km (15 min after decompression), initial signs of decompression disorders are noted — some inhibition and a favoring of the right hind leg.

which developed particularly rapidly during the course of the ascent normally occurred in animals after they had been at depths considerably less than the maximum. The interval between decompression and ascent is of significance in the appearance of the symptoms. Most cases of the gradual development of symptoms at an altitude were observed for brief intervals and were not encountered after the dog had been kept under ordinary conditions for over an hour. Cases of rapid development of





c — 4 min after being at altitude of 4.5 km, signs of decompression disorders progress; d — 6 min after being at altitude of 4.5 km, pronounced decompression symptoms in the right hind leg.

disorders during the course of the ascent occurred both after brief intervals and after intervals as long as 1 hr and 45 min. In the case of ascent to altitude of animals following decompression from increased pressure we noted that the occurrence of pronounced dyspnea and the development of general depression in almost all experiments. The intensity of these symptoms definitely did not correspond to the slight rarefaction of the air used and could not be explained by altitude hypoxemia alone. Both these phenomena were particularly pronounced the greater the increased

Caisson symptoms in dogs during elevations to an altitude of 4.5 km after decompression from increased pressure

No. of experiment	Depth (in m)	Interval between decompression and ascent	Occurrence of symptoms
The dog Zor'ka (28 m)			
1	18	1 h 20 min	—
2	18	15 min	—
3	20	15 min	—
4	18	1 h 40 min	—
5	22	15 min	—
6	24	1 h 20 min	—
7	26	15 min	—
8	26	15 min	7th minute at an altitude
9	26	1 h 40 min	during ascent
10	26	30 min	2nd minute at an altitude
11	26	15 min	—
12	26	1 h 30 min	—
The dog Reks (24 m)			
1	16	1 h	—
2	18	25 min	5th minute at an altitude
3	18	40 min	2nd minute at an altitude
4	18	1 h 20 min	during ascent
5	19	1 h 40 min	—
The dog Sokol (26 m)			
1	18	1 h	—
The dog Valet (22 m)			
1	16	1 h	—
The dog Mishka (22 m)			
1	14	45 min	—
2	14	1 h 20 min	—
3	16	15 min	5th minute at an altitude
4	16	30 min	3rd minute at an altitude
5	18	25 min	—
6	18	30 min	during ascent
7	18	1 h 30 min	—
8	18	1 h 30 min	—
9	18	1 h 40 min	during ascent
10	19	40 min	—
11	22	15 min	3rd minute at an altitude

No. of experiment	Depth (in m)	Interval between decompression and ascent	Occurrence of symptoms
The dog Druzhok (26 m)			
1	12	15 min	—
2	18	45 min	6th minute at an altitude
3	20	30 min	during ascent
4	22	15 min	—
5	22	1 h	7th minute at an altitude
The dog Sedoi (16 m)			
1	16	45 min	—
2	18	45 min	—
3	18	15 min	—
The dog Bogatyr' (22 m)			
1	14	45 min	during ascent
2	14	1 h 40 min	—
3	16	15 min	during ascent
4	16	45 min	during ascent
5	18	15 min	4th minute at an altitude
6	18	1 h 40 min	during ascent
7	20	25 min	—
8	20	30 min	during ascent
9	20	30 min	during ascent
10	20	1 h	—
11	20	2 h	—
The dog Ryzhik (24 m)			
1	14	30 min	—
2	14	45 min	during ascent
3	14	1 h 15 min	—
4	16	16 min	—
5	16	16 min	3rd minute at an altitude
6	18	15 min	5th minute at an altitude
7	18	1 h 30 min	—
8	18	45 min	2nd minute at an altitude

Note. The figures indicated in parenthesis after the name of each dog represent the depth corresponding to the PSC of the animal.

pressure used initially, and the shorter the periods between decompression and ascent to altitude.

Discussion of Results

In our opinion, the most interesting cases were those of rapid development of caisson symptoms in animals during the course of ascent to altitude after having emerged from safe increased pressure. This phenomenon may be explained only by the supposition that prior to the ascent, gas bubbles had already formed at certain places in the body, despite the complete absence of external signs of typical decompression disorders. The immediate and marked appearance of the symptoms which occur in these cases during rarefaction may be explained by only one thing — expansion of gases in a bubble which had already been formed and an increase in its pressure on the surrounding tissues, or, in other words, an increase in the mechanical effects through which the bubble, directly or indirectly, causes painful sensations by interfering with the blood flow. Therefore, consideration of asymptomatic occurrence of caisson disease should include not only the possible formation of small gas bubbles in the moving venous blood stream and asymptomatic air embolism in pulmonary capillaries, but also the presence of "silent" gas bubbles in those places where they exert their physiological influence, producing typical symptoms in the limbs.

It is significant that such gas bubbles — potential causes of symptoms of caisson disease — are found in dogs long after decompression; specifically, they are found even 1 hr and 45 min afterward, when, as a rule, the danger of decompression disorders has passed even if maximum increase of pressure has been applied. It is especially noteworthy that such bubbles were formed in some dogs (Ryzhik, Mishka) even after a pressure of 1.4 atm, i.e., 0.4—0.6 atm below the maximum corresponding to the so-called PSC of the animals. These facts indicate that between the onset of gas formation and the occurrence of typical signs of caisson disease there is a considerable gap, or, in other words, signs of caisson disease initially occurred in the latent form as a rule, and only after reaching a certain intensity did they lead to the development of typical functional disorders.

The second category of cases, where signs of caisson disease developed immediately after reaching altitude, is evidently associated with the formation of gas bubbles under these conditions.

Here it may be supposed that prior to the ascent bubbles did not form at all or were of comparatively small size. Additional decompression naturally activates bubble formation, which leads to the development of functional disorders.

Most cases of gradual development of signs of caisson disease at altitude occur sooner after decompression than in cases of rapid development. This is natural, because rarefaction is a distinctive measure for supersaturation of the body with nitrogen in different periods after decompression. In the late periods the danger of development of decompression phenomena disappears. Here we can expect only caisson

disorders associated with gas bubbles previously formed and localized in typical areas of the limbs, but which had remained latent up to that time.

Data concerning respiratory changes and the general condition of the animals during ascent to altitude after emerging from safe increased pressure deserves special attention. Undoubtedly, both dyspnea and general depression are connected with an increase in the air embolic process during rarefaction; they represent earlier and more constant consequences of supersaturation of the body with nitrogen than the typical joint symptoms of caisson disease. Therefore, in diving practices and caisson work special attention must be given to the general condition of the persons during decompression, to the indices of cardiovascular activity and respiration, and to subjective sensations of general aches and tiredness, which, evidently, inevitably accompany the air embolic process.

Conclusions

1. Under the influence of rarefaction at various periods after decompression from a safe increase in pressure, caisson disease symptoms which develop in animals may be of dual nature: they may occur immediately after the beginning of the ascent, or at various periods after reaching an altitude.

2. After emerging from depths known to be safe, gas bubbles may be formed and preserved for a long time in the body; they are the potential causes of caisson disease symptoms. Thereby there may be no functional disorders whatsoever.

3. Dyspnea and general depression of the body, evidently associated with air embolism, constantly accompany signs of caisson disease; they occur also when caisson disease phenomena do not lead to development of typical decompression disorders in the limbs.

4. Provocation of caisson disorders by means of ascent to altitude is a criterion of the presence of "silent" gas bubbles in the body and the measure of its supersaturation with nitrogen. This method shows promise for further experimental and possibly also practical use.

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P. M. Gramenitskii and A. A. Savich

RESULTS OF EXPERIMENTAL ANALYSIS OF DECOMPRESSION AIR EMBOLISM

(Rezul'taty eksperimental'nogo analiza dekompressionnoi aeroembolii)

There is now no doubt that the air embolic process which begins in the venous capillaries is an essential and possibly the major component in pathogenesis of decompression disorders. Therefore, to understand the mechanism of development of decompression disorders, it is very important to study the conditions which affect gas formation in the blood vessels, the fate of the gas bubbles formed, and the physiological reactions which they induce.

In the literature a great number of observations have been presented on intravital and particularly post mortem gas formation in the body (Ber, 1878; Heller, Mager, Schröter, 1900; Boycott et al, 1908; Harvey et al, 1944; Harvey, 1950; Blinks et al, 1951; Brestkin, 1952; Vavilov and Gramenitskii, 1958; and others). However, a number of problems in this field still remain unsolved: the sequence of appearance of gas bubbles in different blood vessels, the quantitative relationships between gas formation in different parts of the blood stream, the problems of principle in the patency of pulmonary capillaries to air emboli, and the appearance of the latter in the arterial blood.

In the present investigation we attempted to obtain additional data on some of these problems.

Our experiments were divided into two groups: in some experiments we dissected the animals after decompression, and actually observed gas formation in the blood vessels and tissues both before and after the animal had died; in others we used special techniques for demonstrating gas bubbles in the blood (gas traps, centrifugation of blood) and simultaneously recorded changes in respiration and cardiovascular activity in the animals.

Method

Experiments with observation of gas formation in blood vessels were performed on 22 rabbits weighing 2—3.5 kg. The animals were kept in a pressure chamber under a pressure of 2.25 to 5 atm for 6 hrs. Decompression was conducted either at a maximum rate of 10—15 sec or a somewhat reduced rate (50—60 sec). In the former cases, in order to avoid pressure injury to the lungs, an hour before the end of the exposure period

the animals were elevated to the surface with two or three brief stops; a tracheotomy was rapidly performed on them, and they were again subjected to compression prior to the initial pressure effect. At the end of an hour final decompression was performed.

Some of the animals were killed with an electric current immediately upon emerging from increased pressure; others were anesthetized (ether, hexenal), after which they were dissected and a study was made of the blood vessels of the subcutaneous tissue, limbs, abdominal organs, aorta, venae cavae, coronary blood vessels and cardiac chambers. Incidentally, attention was directed to the occurrence of gas bubbles in the fat tissues available to observation.

At the end of the experiment the lungs were tested for pressure trauma; in all cases results were negative.

Experiments with gas traps and centrifugation of the blood were performed on 30 dogs. * The animals under morphine and hexenal anesthesia, with femoral and cervical blood vessels dissected beforehand, were placed in a chamber under a pressure of 3—13.5 atm for different periods of time. The chamber had a forechamber which served as an air lock. In the case of long-term exposure and pressure from 3.0 to 5.0 atm, 30—60 min before decompression two investigators went into the chamber, injected heparin into the animal, and set up the gas traps in the carotid artery and femoral vein. The arrangement and principle of operation of the gas traps are shown in Figure 1.

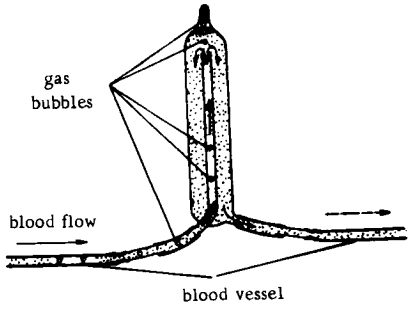


FIGURE 1. Diagram of the gas trap

After setting up the gas traps the investigators left the chamber through the air lock, maintaining the decompression conditions. At the end of the period of action of increased pressure the dog was quickly raised to the surface, where observations were made of gas formation; at the same time a record was made of respiration and blood pressure on a kymograph. In those cases where a pressure of the order of 9—13.5 atm was used, the arterial gas trap was set up before the dog was put into the chamber but opened immediately after decompression. Immediately after it was opened, the gas trap was introduced into the femoral vein.

In six experiments an observation was made of the appearance of gas bubbles in the arterial gas trap after intravenous injection of air into the animals under ordinary pressure conditions. In five experiments, both in the case of decompression and artificial air embolism, centrifugation of the arterial blood was performed so that when it was separated into its various fractions, small bubbles invisible to the naked eye would float up and appear over the clear layer of plasma. For this purpose, both outlets of the gas traps, entirely filled with blood, were closed with small stoppers; upon centrifugation the latter were directed toward the center of rotation. A study was made of a control sample of blood taken before the animal was put into the chamber and of two or three samples taken after decompression.

* In the performance of some of these experiments N. Ya. Sidorov and K. S. Yurova participated.

Results of the Experiments

In all experiments with observation of the blood vessels of animals killed and dissected immediately after decompression (pressures of 2.25, 2.5, 2.75, 3.0, 3.25, and 5.0 atm and exposure of 6 hrs) we noted without exception the appearance of gas bubbles both in the veins and in the arteries. The number of gas bubbles depended on the pressure used in the experiments: at 2.25 atm they could easily be counted in one or another of the blood vessels; with increase in the pressure by 1/4 atm their number increased, and at 3.25 atm they were present in large numbers; finally, at 5 atm the blood vessels were solidly filled with gas.

The first gas bubbles in the blood vessels which were visible at pressures of 3.25—2.25 atm appeared 3—10 min after decompression, and at pressures of 5 atm they were found immediately after dissection.

With respect to the intensity of gas formation in these experiments it is difficult to say that any one area of blood vessels was particularly affected; it is important to emphasize that here, as a rule, there was no great difference between arteries and veins. In some experiments it was found that gas formation in the arteries began earlier and proceeded more actively than in the corresponding veins. To exclude the possibility of gas bubbles passing through arteriovenous anastomoses, we isolated various sections of arteries and veins with ligatures in a number of experiments. In all cases where the isolated sections of various blood vessels were not exceedingly small, gas formation occurred both in the venous and arterial blood.

In experiments on anesthetized rabbits which, while still alive, were dissected immediately after decompression, gas formation in the venous blood was also observed without exception. The only difference from previous experiments was that gas bubbles appeared somewhat later, in smaller numbers, and chiefly in the veins carrying blood from the tissues rich in fat.

Because it was impossible to observe gas bubbles in the arteries during the movement of blood, we ligated the arteries at various periods after decompression. In some cases the abdominal aorta was ligated under the diaphragm; at the same time a ligature was applied to the vena cava at the same level and in this way the blood flow was stopped in the entire hind part of the animal's body. In other cases the femoral arteries and veins, the renal arteries and veins, the branches of the mesenteric arteries and veins were ligated. In addition, a section of the abdominal aorta without branches or sections of the mesenteric arteries were almost always isolated between two ligatures.

The experiments showed that when the ligatures were applied in the first 10—15 min after decompression gas bubbles always appeared in the ligated arteries, including those sections which were completely isolated. While initially small, the bubbles gradually grew larger, developing into gas accumulations in a number of cases. Under conditions which were otherwise the same, gas formation proved to be more active the earlier the blood flow was stopped; when the ligature was applied the first 3 min after decompression, its intensity in the arteries was even somewhat greater, as a rule, than in the veins ligated in a similar way.

At a pressure of 3.25 atm, a 15 minute period after decompression was the maximum for intra-arterial gas formation; gas bubbles never

occurred in arteries ligated after this time. Appearance of bubbles in the venous blood, both in nonligated and ligated blood vessels, could be observed for a few score minutes after this. Gas formation in the fat tissues (fatty tissues surrounding the mesenteric blood vessels, retroperitoneal, and subcutaneous fat), was distinct only after the animals had been under pressure exceeding 3 atm.

In experiments on dogs with the use of gas traps, initially a pressure of 3 atm was applied with a 6 hour exposure (five experiments). In all cases 5—8 min after decompression gas bubbles began to appear in the venous gas traps; their number increased so rapidly that shortly afterward the upper portion was filled with a layer of fine bloody foam. Gas formation in the venous blood increased in the first 15—20 min; beginning with the 30th—35th minute there was a gradual reduction, and 1—1.5 hrs later it had almost completely disappeared. In three out of five experiments we observed small numbers (10—20) of gas bubbles in the arterial gas trap in the 10th—12th minute after decompression; subsequently their number did not increase; all five animals survived caisson disease.

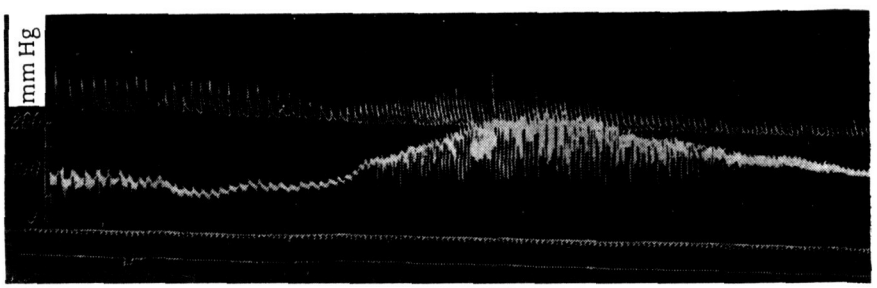


FIGURE 2. Change in respiration and circulation of a dog with decompression air embolism. The beginning of the record was made 12 min after decompression (pressure and exposure time as follows: 5 atm, 20 min; 4 atm, 2 hrs; 3 atm, 1 hr 30 min; 4 atm, 1 hr 30 min). Experiment of 12 May 1959.

From top down: respiration, blood pressure in the femoral artery; time marking, 3-second intervals; base line of the blood pressure. The blood pressure at the beginning of the record was 110 mm. The mark on the bottom curve represents the opening of the arterial gas trap; the arrow indicates the appearance of bubbles in the arterial blood.

In the other 15 experiments pressures from 5—13.5 atm were used with different exposure times. The results of these experiments are shown in the table, from which it is evident that in five cases accompanied by moderate or slight gas formation in the venous blood, bubbles were not found in the arterial gas trap. In the other 10 experiments, together with a vigorous gas formation in the veins, gas bubbles also appeared in the arterial blood. In some experiments they were occasional; in the majority they came to several score. In those cases where rapid death of the animals did not occur, the appearance of gas bubbles in the arterial blood stopped after a certain time (usually 12—20 min); in the venous blood vigorous gas formation continued.

Changes in the respiratory and cardiovascular activity of the animals were, in general, typical of pronounced caisson disease and essentially fit the picture described previously by I. I. Vavilov and P. M. Gramenitskii (1958). However, a comparison of these functional changes when gas forms in the arterial blood showed the following curious fact: when a considerable number of gas bubbles was noted in the arterial gas trap a pronounced and quite long-lasting pressor reaction usually occurred, against a background of bradycardia, with periodic marked increases in the heart rate (Figure 2).

After intravenous injection of air into the animals at ordinary pressure we never observed the appearance of gas bubbles in the arterial gas trap, even though the air had been introduced in large quantities and the dogs ultimately died of air embolism.

Centrifugation of the arterial blood was unjustified from the methodological viewpoint and failed to give distinct results.

Discussion of Results

The experiments performed confirmed the principle already known that the air embolic process in the venous system represents the basic phenomenon in pathogenesis of overt decompression disorders. At the same time, new facts were obtained dealing with the appearance of gas bubbles in the arterial blood during decompression disorders.

It is not surprising that intense gas formation occurs not only in the venous but also in the arterial blood of animals killed immediately after rapid decompression from pressures of 2.25 atm or more. During the short period of actual decompression and the 15—30 sec which elapsed at the surface before the animal's death no considerable desaturation could have occurred, and all the body tissues including the arterial blood were equally supersaturated with nitrogen. True, if we consider that the arterial blood comes to equilibrium with alveolar air with respect to nitrogen diffusion just as quickly as with respect to oxygen or carbon dioxide diffusion, i.e., almost instantaneously we might expect, under these conditions, a somewhat lesser degree of gas formation in the arterial blood than in the venous blood. However, the experiments did not show this. The fact that gas bubbles and accumulations did appear in the stopped arterial blood when the arteries were ligated comparably long periods (up to 15 min) after decompression is most interesting and, it might be said, unexpected. As has already been pointed out, visible gas bubbles do not appear immediately after application of the ligatures, and once they appear, they continue to increase in size steadily. Therefore, this was not a matter of ligation of the arteries and stoppage of their blood flow permitting the detection of gas bubbles which had previously formed in the arterial blood; this was undoubtedly a matter of gas formation within the arterial vessels.

True enough, experiments with gas traps lead us to suppose that in the arterial blood in the presence of overt signs of caisson disease, sometimes with occasional bubbles visible to the naked eye, there may also be a quite large number of microscopic "gas embryos". However,

Results of experiments on dogs with the use of gas traps

Date of experiment	Weight (in g)	Pressure (in atm) and exposure time (in min)	Observation of the appearance of bubbles (in minutes after the end of decompression) in the gas trap						Outcome of the experiment
			in the arterial blood			in the venous blood			
			beginning	maximum	end	beginning	maximum	end	
12 V 1959	20	5.0 (20), 4.0 (120), 3.0 (90), 4.0 (90)	13	20-22	30-35	5	8-12	Gas formation continued until the end of the experiment	2 hrs and 20 min after decompression the animal was killed by asphyxiation
22 IV	22	5.0 (300), 4.0 (28), 5.0 (60)	Immediately after opening the gas traps there were a tremendous number of bubbles						Death in the 14th minute from caisson disease
14 V	22	5.0 (140), 3.0 (30), 4.0 (20)	7	10	10	4	15	The quantity of gas increased steadily	Death in the 27th minute from caisson disease
18 VI 1958	10.3 (puppy)	7.0 (30)	No gas formation			Large number of bubble immediately		In the 50th minute	Killed by asphyxiation 2 hrs 30 min after decompression
21 V 1959	22	8.0 (35), 3.0 (30) 6.0 (80)	3	7-12	20	8		Gas formation progressed until the end of the experiment	Death in the 45th minute from caisson disease
25 V	27 (fat animal)	9.0 (10)	No gas formation			10		Gas formation progressed until the end of the experiment	Death in the 25th minute from caisson disease
28 V	25	9.0 (10)	No gas formation		5	40		Continued until the end of the experiment	Killed by asphyxiation 2 hrs after decompression
4 VI	20	9.0 (20)	4	Uniformly intense gas formation until animal's death		4		Uniformly intense gas formation until animal's death	Death in the 18th minute from caisson disease
6 VI	18.9	9.0 (20)	4	5	19-20	Immediately	40-45	Continued until the end of the experiment	Killed by asphyxiation 2 hrs 30 min after decompression

Date of experiment	Weight (in g)	Pressure (in atm) and exposure time (in min)	Observation of the appearance of bubbles (in minutes after the end of decompression) in the gas trap						Outcome of the experiment
			in the arterial blood			in the venous blood			
			beginning	maximum	end	beginning	maximum	end	
23 VI	24	9.0 (30)	Immediately	7-8	Continued until the end of the experiment	Immediately	Gas formation progressed until the end of the experiment		Death in the 13th minte from caisson disease
25 VI	18.5	9.0 (30)	4	7-8	12	Injected 10 min after decompression. Abundant gas formation until the end of the experiment			Death in the 13th minute from caisson disease
9 VI 1959	10	13.5 (8)	No gas formation						Killed by asphyxiation 3 hrs after decompression
13 VI 1959	23.5	13.5 (15)	Immediately	4-5	Continued until end of experiment	Gas trap not introduced; a multitude of bubbles in the veins			Death in the 14th minute from caisson disease
11 VI 1959	23	13.5 (20)	Immediately	Gas formation progressed till death of animal		Gas trap not introduced; a multitude of bubbles in the veins			Death in the 7th minute from caisson disease
16 VI 1959	20.5	13.5 (15)	No gas formation			7	50	Continued until the end of the experiment	Killed by asphyxiation 2 hrs and 20 min after decompression

even here, the fact that no large quantities of gas are formed in the ligated artery is beyond doubt.

The reasons for this gas formation may be reduced to three circumstances: because of slow diffusion of nitrogen in the lungs the arterial blood as a whole remains supersaturated with it in the periods indicated after decompression, or the formed elements of the blood which desaturate more slowly than plasma furnish the nitrogen, or the nitrogen diffuses into the stopped blood from the arterial walls, which, incidentally, are rich in lipoids which readily dissolve indifferent gases.

These three possible causes of gas formation in the ligated arteries may well operate simultaneously. In any case, the results of the experiments leave no doubt that in these situations (rapid decompression from pressures of 2.25—3.25 atm after a 6 hour exposure period) there are all the conditions for gas formation in the arterial blood (in the arteries) 10—15 min after decompression.

Evidently, the only factor preventing the realization of these conditions in the intact organism, as was the case in our experiments, is the rapid movement of arterial blood. For the formation of visible gas bubbles in a supersaturated solution a time measured in minutes is required, whereas a certain portion of the arterial blood traverses its entire route from the pulmonary capillaries to the capillaries of even the furthest parts of the body in a period measured in seconds. This time is clearly inadequate for microscopic gas bubbles or "gas embryos" formed in the blood itself and passing through the pulmonary capillaries to increase to a large size.

Relatively large gas bubbles in the moving arterial blood evidently can be formed only when there are severe degrees of supersaturation of the body with the indifferent gas. Apparently, our experiments with gas traps attest to this. However, in connection with everything stated, the results cannot be evaluated categorically: a considerable slowing of the blood flow in the gas trap may have played a part in the appearance of gas bubbles visible to the eye.

The facts obtained make us take a somewhat different approach to the problem of decompression air embolic phenomena in the arterial system.

Sources in the literature usually pose this problem in the following manner: If the pulmonary capillaries are patent to gas bubbles, as Fotakis, L'Hermite and Hasseigne and Pines (quoted by Yakobson, 1950) believe, the appearance of gas bubbles in the arterial blood is entirely possible; if the pulmonary capillaries are not patent, as the majority of investigators (Magendie, 1821; Shestopal, 1898; Miram, 1909; Il'in, 1914, and others) state, there should be no gas bubbles. Such a formulation of the problem is, in our opinion, unjustified. Undoubtedly, the pulmonary capillaries, in contrast to the vascular system of the greater circulation, do not permit the passage of large bubbles visible to the eye, but this does not at all mean that they are absolutely nonpatent to air emboli. The latter, after blocking the capillaries, decrease in size because of nitrogen diffusion into the alveolar space, and become smaller than the capillary diameter. Then, by force of the blood pressure, they should inevitably be carried into the pulmonary veins.

If the arterial blood is not supersaturated with nitrogen, microscopic gas bubbles may be dissolved in the plasma, as pointed out by A. P. Brestkin (1953), because of excess pressure in them which increases with volume reduction.

Evidently, because of the self-destruction of subcapillary gas bubbles passing through the pulmonary vascular system, under ordinary conditions we never find air in the arterial blood after it has been introduced into the veins.

A different situation arises in decompression air embolism. Here, as experiments have shown, for many minutes after decompression the arterial blood continues to be supersaturated with nitrogen, and all conditions are present for the expansion of gas "embryos" which have passed through the pulmonary capillaries. However, because of the rapid movement of arterial blood the gas bubbles in it cannot expand to a large size, and, as a rule, no air embolism occurs in the arterial branches of the greater circulation, particularly since they are considerably more patent to gas bubbles than the pulmonary capillaries.

On the basis of everything stated, we can represent the development of air embolism when the body is considerably supersaturated with nitrogen initially after decompression in the following way. Large masses of gas constantly formed in the slow-moving venous blood are retained in the pulmonary capillaries, where diffusion of nitrogen from the air emboli into the alveolar space occurs. Microscopic gas bubbles constantly penetrate into the arterial blood through the pulmonary vascular system; because of the supersaturation existing here they begin to expand, but because of the rapidity of the blood flow, they do not reach a large size, and they enter the tissue capillaries, where they meet all the conditions for further increase in size. Therefore, progressively newer portions of gas come to the lungs; they are retained and, to a considerable degree, eliminated there, and only the smallest gas bubbles pass through the arterial system constantly. It is significant that the possibility of their enlargement to dangerous embolic size is determined by the time of passage of the arterial blood to one part of the body or another. Such a danger is less threatening to organs located closer to the heart, and, evidently, is practically impossible for the heart muscle itself.

In conclusion, it should be noted that the most important idea stemming from the facts obtained is that of slow nitrogen diffusion. This requires the most immediate experimental verification, because it deals with the fundamental question of the entire problem of decompression disorders — the rate of saturation and desaturation of the body as a whole and of its separate tissues.

Conclusions

1. When rabbits were killed immediately after decompression from a pressure of 2.25 atm or more after a 6 hour exposure, pronounced gas formation occurred in the veins and arteries of various parts of the body.

2. Under similar conditions in living rabbits after ligation of arteries, carried out in the first 15 min after decompression and in completely isolated sections of arteries, gas bubbles and an accumulation of gas are found.

3. With active post-decompression gas formation in the venous blood of dogs, gas bubbles usually appear in the gas trap introduced into the carotid artery, and are associated with an increase in blood pressure and bradycardia.

4. After air is intravenously injected, it cannot be found in the arterial blood.

5. When the body is considerably supersaturated with nitrogen, for a comparatively long time after decompression (at 3.25 atm, 15 min) all conditions are present for gas formation in the artery. However, because of the rapid flow of the arterial blood the gas bubbles in it usually do not manage to increase to visible size.

6. The data obtained suggests the idea of slow nitrogen diffusion in the lungs and, evidently, in the tissues.

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P. M. Gramenitskii, A. A. Savich, and K. S. Yurova

THE EFFECT OF DIFFERENT GASES ON THE ORGANISM AFTER INTRAVENOUS ADMINISTRATION

(Deistvie na organizm razlichnykh gazov pri ikh vnutrivennom vvedenii)

As determined by A. P. Brestkin (1958), blood is much less able to retain nitrogen in a supersaturated solution than other body tissues. Because of this, when decompression exceeds the limit of the permissible change in pressure, gas formation occurs with particular ease in venous blood, which is supersaturated with nitrogen diffusing into it from the tissues. The studies of I. I. Vavilov and P. M. Gramenitskii (1958) show that air embolism of the venous system and pulmonary blood vessels is the central phenomenon in the pathogenesis of decompression disorders.

On this basis, it was interesting to study the body's reactions to injections of various gases into the venous blood, because in actual cases of caisson disease gas bubbles may differ considerably, depending on the gas mixture breathed before decompression, as well as on the absolute pressures under which the decompression disorders developed. The lower this pressure, the more readily the bubbles of indifferent gas (nitrogen or helium), molecules of carbon dioxide or oxygen, will diffuse. Therefore, it was interesting to investigate the effect of each of these gases separately, as well as air and a helium-oxygen mixture, which are used for breathing in underwater descents.

Method

In all, 68 short-term experiments were performed on 50 cats and 18 rabbits, and 15 long-term experiments were performed on rabbits. A short-term experiment was performed under hexenal anesthesia. A kymographic record was made by the usual method of respiration and blood pressure in the left femoral artery. A cannula was inserted into the right femoral vein for the introduction of gas. The latter was carried out by means of a special system, consisting of a large (3 liter) funnel from a gas meter and a glass burette of 15 ml, which were connected by a rubber tube, with a screw clamp regulating its lumen. This system of connecting vessels was filled with water. A rubber tube connected to the venous cannula during the introduction of the gas was set on the upper end of the burette. This tube and the burette were filled to the top mark with one gas or another and the screw clamp was tightly closed; the funnel with

the fluid was placed 20 cm above the burette. The system was connected with the venous cannula. On opening the screw clamp the gas began to enter the vein under the pressure of the fluid. The rate of its introduction could be regulated accurately, In a number of short-term experiments the animals breathed oxygen or a helium-oxygen mixture during the injection of the gases. In these cases a tracheotomy was performed. and respiration was carried out through a miniature valve box connected to the tracheotomy tube. In 14 experiments a comparison was made between the reactions to intravenous gas injection in animals with an intact nervous system and those in animals whose vagus nerve had been severed in the neck.

In all, 15 injections of carbon dioxide, 40 of oxygen, 90 of air and 26 of the helium-oxygen mixture were given. The rate of administration of the gases and the sequence with which they were used differed in various cases depending on the aims of the experiment. In the long-term experiments the gases were introduced into the auricular veins of rabbits, after which the condition and behavior of the animals were observed.

Results of the Experiments

The respiratory and circulatory reactions to the intravenous injection of indifferent gases (nitrogen, helium, and an 80 % mixture of each gas with oxygen) were very similar to those noted during development of decompression air embolism (Vavilov and Gramenitskii, 1958). In both cases the situation amounted essentially to a gradual increase in dyspnea with characteristic periodic deep and sudden inspirations, a steadily progressive drop in blood pressure, and bradycardia occurring shortly after the administration of the gas in most cases. Cutting the vagus nerves in the neck eliminates bradycardia but not dyspnea. With continued administration of the gas in lethal quantities, respiration is inhibited and then stops in the preagonal period; the blood pressure drops to critical levels, and following respiratory arrest, the cardiac activity stops after a number of arrhythmical — now weak, now strong — heart beats.

As the short-term experiments showed, different gases vary greatly in the degrees of their effects after intravenous administration. It was found that the body suffers most severely from intravenous air injection, tolerates the administration of helium and the helium-oxygen mixture better, that of oxygen much better and, finally, that of carbon dioxide particularly well. These relationships are illustrated by the kymograms presented below.

It should be noted that the effects presented on the kymograms refer to cats, which, as the experiments showed, are incomparably more resistant to the intravenous administration of gas than rabbits. Thus, for rabbits the injection of even 1.0—1.5 ml of air in 30 sec was lethal, whereas cats can tolerate an injection of 10—15 ml of air at a rate of 1 ml in 20 sec.

On Figure 1 the effect of an injection of 14 ml of air into the femoral vein of the cat at the rate of 1 ml in 14 sec is shown. As a result, after brief inhibition of respiration, dyspnea occurred, and the blood pressure

dropped from 110 to 25 mm. At the end of the administration gradual functional recover was noted, but even 27 min after the injection (the last record on the right) the blood pressure had not returned to the initial level.

In Figure 2 the effect of the injection of the same quantity of helium at a somewhat greater rate (1 ml in 12 sec) is shown. As the kymogram shows, changes in respiration and cardiovascular activity were less pronounced.

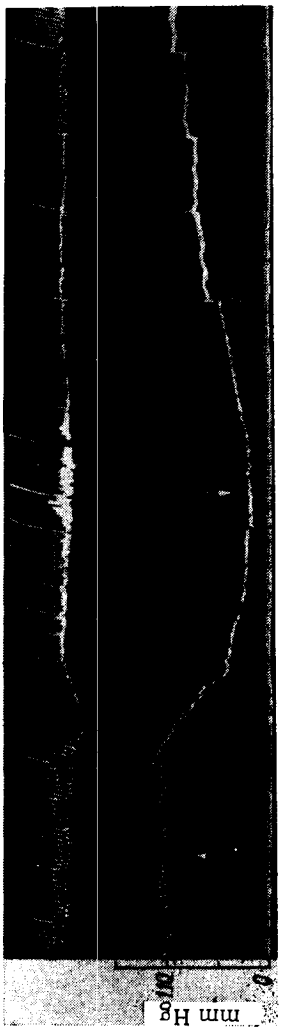


FIGURE 1. Change in respiration and blood pressure in an anesthetized cat after the intravenous administration of 14 ml of air at the rate of 1 ml in 14 sec

From top down: respiration, blood pressure in the femoral artery; time marking (1 second intervals); base line of the blood pressure. The arrows, from left to right, designate the beginning and end of air administration; the figures under the pressure curve show the time of interruption of the record (in minutes).

The blood pressure dropped from 112 mm to 40 mm, but as early as 3 minutes afterwards it had almost returned to the initial level.

Figure 3 shows the effect of oxygen injected into the vein at a rate of 1 ml in 13 sec. The initial abrupt blood pressure drop is explained by an increase in the rate of gas administration. After the administration of 14 ml of oxygen, as the kymogram shows, no marked changes are noted in respiration or blood pressure. Critical functional disorders occurred only after the administration of 41 ml of oxygen.

Experiments with intravenous injection of carbon dioxide at the same rate showed that the animals can compensate for this effect indefinitely. Thereby the blood pressure does not change appreciably, and only a uniform and active dyspnea occurs.

As shown in Figure 4, even the sudden intravenous injection of very large quantities of carbon dioxide (32 ml in 12 sec) causes only a brief blood pressure drop and very transitory respiratory changes; functioning returned to normal in the next few minutes.

It was found that the ease with which the body tolerates intravenous injection of one gas or another depends to a considerable degree on the diffusion relationships created in the lungs. Thus, if the animal is made to breath oxygen it tolerates the intravenous injection of oxygen less well than under ordinary conditions, i. e., during the breathing of air. The administration of air while breathing oxygen is, conversely, tolerated appreciably better. Likewise, intravenous injection of helium is less easily tolerated when the animal breathes a helium-oxygen mixture rather than ordinary air, and better tolerated when the

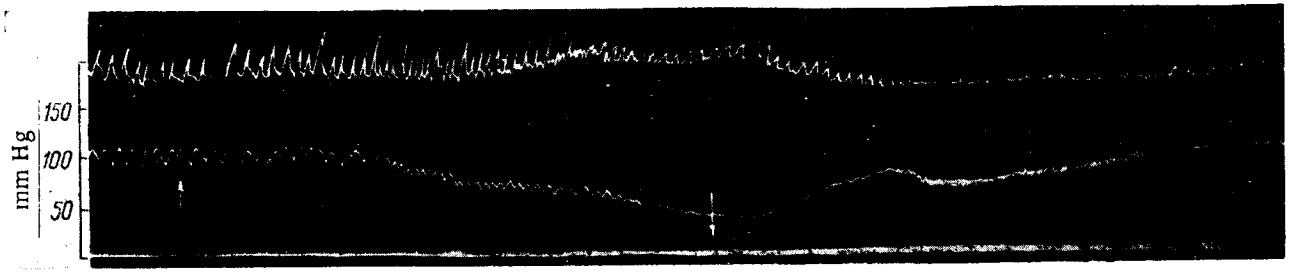


FIGURE 2. Change in respiration and blood pressure in an anesthetized cat after intravenous administration of 14 ml of helium at the rate of 1 ml in 12 sec

The key is the same as for Figure 1.



FIGURE 3. Change in respiration and blood pressure in an anesthetized cat after intravenous administration of oxygen at the rate of 1 ml in 13 sec

The arrows (from left to right): beginning of administration of 14 ml of oxygen; beginning of additional administration of 27 ml of oxygen; end of oxygen administration. The rest of the key is the same as for Figure 1.

animals breathe oxygen. However, it should be noted that after intravenous administration of gases the role of these diffusion relationships are clear only up to a certain time during the injection, i. e., before the air embolic phenomena reach a considerable degree of severity and assume threatening proportions. In the same period, regardless of the nature of the gas injected into the vein, inhalation of oxygen is always useful.

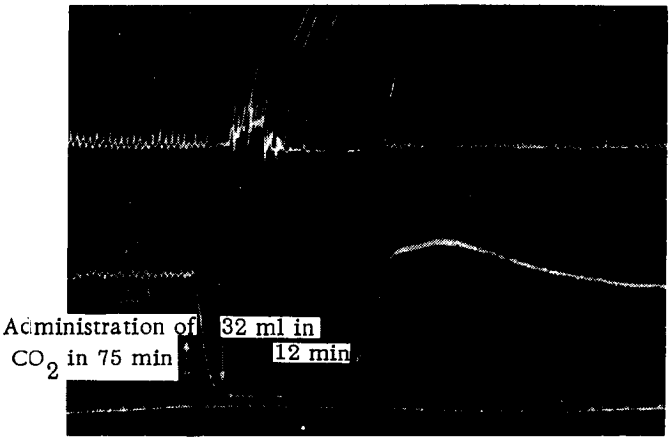


FIGURE 4. Change in respiration and blood pressure in an anesthetized cat after intravenous administration of 32 ml of carbon dioxide in 12 sec

The key is the same as for Figure 1.

The experiments showed, however, that the different effects of these various gases cannot be explained simply by diffusion relationships created in the lungs; they depend also on the properties (diffusion power) of the gases themselves. Thus, air administration while breathing air is less well tolerated than a helium-oxygen (21% oxygen) mixture while breathing the same mixture, and much more poorly than the administration of oxygen while breathing oxygen.

In observations of vagotomized animals during intravenous gas administration we gained the impression that cutting the vagus nerves increases body resistance to air embolism. However, the very great individual differences in the animals' resistance to this effect interfered with drawing any categorical conclusions in these experiments.

Long-term experiments performed on rabbits completely confirmed the differences noted above and the interrelationships of physiological effects of intravenous administration of the four gases investigated.

Discussion of Results

The great similarity between respiratory and circulatory changes found after intravenous administration of gases and those associated with overt decompression disorders confirms the leading role of air embolism in

the venous system and pulmonary capillaries in the origin of these disorders. Hence it follows that artificial air embolism is a good model of general decompression disorders and may be used advantageously for the study of the mechanisms of their occurrence and development.

It also follows that essential differences in the physiological effects of the different gases when given intravenously, which have been found in a number of experiments, must, of necessity, be considered in the analysis of caisson disease phenomena encountered in diving practice.

Differences in the effects of various gases are evidently associated with two circumstances. The first involves chemically active gases — oxygen and carbon dioxide — which, when they are injected into the blood stream, can be more or less bound by substances present there (oxygen, by hemoglobin; carbon dioxide, by alkalis).

The second circumstance applies to all the investigated gases and amounts to their different diffusion capacities. As is well known, carbon dioxide has a much greater power of diffusion than oxygen; helium, much greater than nitrogen. For the last two gases, which are chemically indifferent, the difference in the diffusion capacity is evidently decisive and the sole reason for the differences in degrees of their physiological effect. The course and outcome of artificial air embolism will depend chiefly on how quickly the gas bubbles entering and obstructing the pulmonary capillaries are eliminated. Their elimination is determined by the rate of gas diffusion from these bubbles into the alveolar space. Helium has a milder physiological effect than nitrogen because, due to its greater power of diffusion, helium-air emboli are more rapidly eliminated by the body.

This fact may explain the apparent discrepancy between A. P. Brestkin's data (1958) concerning the permissible supersaturation coefficient of solutions with helium and nitrogen, and the results of studies of the permissible supersaturation coefficient of the human body with these gases which he made in cooperation with I. A. Aleksandrov (1963). A. P. Brestkin's experiments with in vitro solutions showed that helium forms bubbles in solution with a lesser degree of supersaturation than nitrogen; in the investigations of A. P. Brestkin and I. A. Aleksandrov it was determined that the development of caisson disease symptoms in persons who have been under increased pressure occurs at a greater supersaturation when they breathe helium-oxygen than when they breathe air. Probably, when the body is supersaturated with helium, gas bubbles form more easily than in the case of nitrogen supersaturation, but because of the greater stability of the nitrogen bubbles, decompression symptoms during the breathing of air develop with a lesser degree of supersaturation.

In the light of the above, the significance of the diffusion relationships between air emboli and the alveolar air studied in our experiments becomes quite understandable. Air emboli made up of a different gas than that which fills the alveolar space will be eliminated by diffusion more rapidly than air emboli of a composition similar to the alveolar air, under conditions which are otherwise the same.

The results obtained in the experiments lead us once again to direct attention to the use of oxygen for decompression air embolism, on which P. Ber insisted (1878).

The fact that with far-advanced air embolism, oxygen is more beneficial even though its intravenous administration causes functional disorders,

and disadvantageous diffusion relationships are apparently created in the lungs, is explained evidently by the development of pronounced hypoxemia due to blockage of a large number of pulmonary capillaries with gas bubbles. The nature of the gas blocking the capillary is evidently not of great importance for the development of hypoxemia, and the latter, with a certain degree of air embolism in the pulmonary vessels, always becomes a general and most significant phenomenon in the pathogenesis of decompression disorders.

Conclusions

1. Changes in respiration and circulation occurring in animals after intravenous injection of different gases are very similar to changes in these functions in the presence of pronounced compression disorders. This is evidence of the leading role of air embolism of the venous system and pulmonary vessels in the development of general decompression disorders.

2. Different gases vary greatly in the strength of their physiological effects after intravenous injection. The body suffers most severely from the intravenous injection of nitrogen; it tolerates intravenous injection of helium appreciably better; of oxygen, even better; and of carbon dioxide, particularly easily. This is explained by the different diffusion capacities of these gases, and, in the case of oxygen and carbon dioxide, also by the possibility of their chemical combination in the body.

3. The results of artificial air embolism depend to a great degree on the diffusion relationships created in the lungs between the air and the gas mixture filling the alveoli. Hence, it follows that in the elimination of air emboli the leading part is played by diffusion of their constituent gases from the pulmonary vessels into the alveoli.

4. The facts listed above should be taken into consideration in the analysis and treatment of decompression disorders.

5. Artificial air embolism can constitute an experimental model for general decompression disorders.

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P. M. Gramenitskii and K. S. Yurova

TRAINING OF THE ORGANISM FOR ARTIFICIAL AIR EMBOLISM

(Trenirovka organizma k iskusstvennoi aeroembolii)

In the experiments of V. A. Aver'yanov, P. M. Gramenitskii and A. A. Savich (1961) it was determined that in dogs repeatedly exposed to the effects of decompression after emerging from increased pressure, an increased resistance to decompression disorders occurred. In this connection, the problem naturally arose of the basis and physiological mechanisms of this phenomenon.

All existing data on the subject permits us to suppose that this increased resistance is based, to a considerable degree, on the perfection of the body's reactions to decompression embolism. Gas formation in the blood in overt decompression disorders has been noted by the majority of investigators working on this problem (Ber, 1878; Heller, Mager, and Schrötter, 1900; Boycott, Damant and Haldane, 1908; Hill, 1912; Harvey, Burnes, et al, 1944; Yakobson, 1950; Blinks, Twitti, and Whitaker, 1951; and others). From the works of A. P. Brestkin (1958), I. I. Vavilov and P. M. Gramenitskii (1958) and from the recent studies of P. M. Gramenitskii, A. A. Savich, and K. S. Yurova (1964), it follows that air embolism is a central factor in decompression disorders and always precedes and accompanies the development of typical caisson disease symptoms in the limbs. At a certain intensity, the air embolism, which develops essentially in the venous blood and pulmonary vessels, undoubtedly causes a number of respiratory and circulatory reflex reactions, among which are those contributing to the elimination of gas bubbles already formed in the blood, and preventing the formation of new ones. There is also no doubt that the condition of respiration and circulation directly affects desaturation of the tissues with respect to the indifferent gas, gas formation in the tissues, and resorption of already formed extravascular gas bubbles. All the above supports the idea that general increase in resistance to decompression disorders is based on perfection of compensatory reactions of the body to air embolism. The present work was undertaken to check this idea, mainly by determining the possibility of increasing body resistance to air embolism, by means of regularly repeated intravenous injections of air into animals, in doses which do not cause serious functional disorders.

Method

The experiments were performed on 32 rabbits, half of which served for the control experiments.

In all cases air was injected into the auricular veins of the rabbits from a well- ground syringe through a fine needle at a rate of 1 ml in 15 sec. At the end of the injection the animals were placed on the table without fixation and observed continuously for 2 hrs.

Results of the Experiments

We first determined which doses of air caused the initial, very transitory functional changes, which produced overt disorders, and finally, which led to irreversible disorders and death. The first reactions, in the form of slight dyspnea and some general inhibition of the animal, were found after an injection of 0.5—0.6 ml of air. Doses of 1.0 ml caused pronounced dyspnea, general depression, and sometimes mild, very transitory paresis of the hind legs. After the injection of 1.3 ml of air, dyspnea and general depression were more pronounced and signs of opisthotonos and paresis of both hind legs occurred. All these phenomena usually disappeared without trace in time; only in some cases did the rabbits die. Doses of 1.5 ml of air were lethal to the majority of animals; in the agonal period generalized convulsions appeared. Finally, an injection of air in quantities of 2.0 ml or more is undoubtedly lethal to the rabbits. It should be emphasized that even after the administration of doses of air known to be lethal, in almost all animals paralysis of the hind legs develops together with general depression and marked dyspnea; the forelegs are always paralyzed last, if at all. Figures 1, 2, and 3 show the conditions of the rabbits after the injection of different quantities of air.

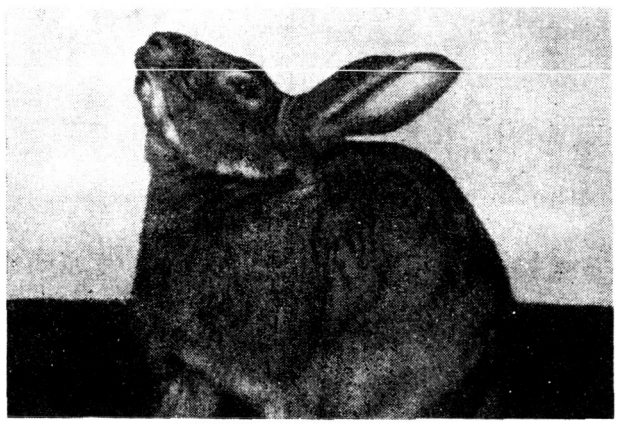


FIGURE 1. Rabbit No. 12, three minutes after intravenous injection of 1.3 ml of air

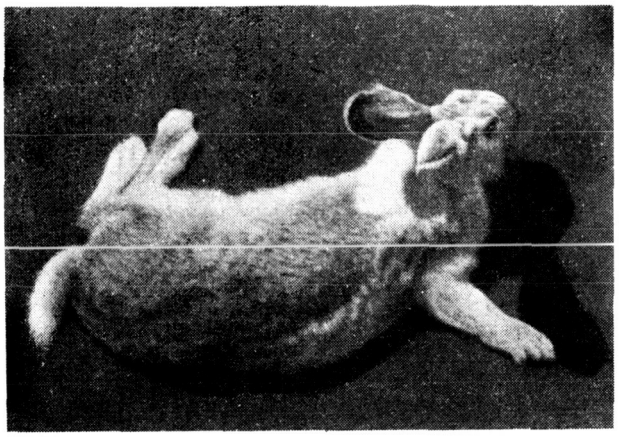


FIGURE 2. Rabbit No. 7, eight minutes after intravenous injection of 1.5 ml of air



FIGURE 3. Rabbit No. 2, two minutes after intravenous injection of 3 ml of air

In Table 1 the results of the control experiments are presented.

After determining the lethal doses of air in the control experiments we began the main experiments. The procedure for them was as follows: Initially, for the purpose of evaluating the basic reactions, each rabbit was given 1.2—1.3 ml of air. After this, for a number of days the rabbit was given threshold doses (0.6 ml) and then increased doses, 1, 2, and 3 times each day (with repeated injections at 2 hour intervals). Finally, the action of doses known to be lethal was checked. The results of the experiments, given in Table 2, show a definite increase in the resistance of the rabbits to the harmful effect of air embolism as a result of repeated regular injections of air, beginning with comparatively small doses. Even during the experiments, after a number of injections of air in threshold doses (0.6 ml), the rabbits acquire the capacity of tolerating doses of

1.0, 1.5 and even 2 ml equally well (Table 2, rabbits Nos. 3, 4, 6, 7 and 8). Consequently, the animals can tolerate quantities of air known to be lethal. Thus, in six cases the rabbits withstood an injection of over 4 ml; two of them (Nos. 6 and 7), 6.5 and 8 ml, i.e., doses more than 4 times greater than the median lethal doses. This data indicates the possibility of a unique training of the body to such an unusual effect as the intravenous injection of gases.

TABLE 1

Results of intravenous injection of different doses of air into rabbits in control experiments

No. of experiment	Quantity of air injected (in ml)	Reaction of the body to the injection of air and outcome of the experiment
1	9	Generalized tonic convulsions. Death in the 3rd minute
2	3	Paralysis of the hind legs and then of the forelegs. Death in the 3rd minute
3	3	The same reaction. Death in the 5th minute
4	3	Very marked general depression and then paralysis of the hind legs and opisthotonus. Death in the 16th minute
5	2	Opisthotonus and generalized convulsions. Death in the 3rd minute
6	1.5	The same reaction. Death in the 5th minute
7	1.5	Steadily progressive dyspnea and paralysis of the hind legs. Death in the 17th minute
8	1.5	The same reactions. Death in the 12th minute
9	1.8	Paralysis of the hind legs, chronic convulsions of the anterior part of the body. Death in the 4th minute
10	1.3	Marked dyspnea, opisthotonos, paralysis of the hind legs. Death in the 6th minute
11	1.3	Dyspnea, paresis of the hind legs. Survived
12	1.3	Dyspnea, general depression. Opisthotonos. All survived
13	1.0	Pronounced dyspnea, general inhibition. Survived
14	0.6	Dyspnea, very slight inhibition. Survived
15	0.5	The same
16	0.3	No apparent change

Our fears of cumulative effects, particularly when animals were given three portions of air daily over a number of days (rabbits Nos. 10 and 11), were completely dispelled by the experiments, which showed that after 3 injections of air daily the effect of increased resistance was greatest.

Specially performed experiments (18 experiments on five rabbits) to determine how quickly the body eliminated air emboli introduced into the blood are of interest in this connection. At various periods (5 min to 2 hrs) after the intravenous injection of readily tolerated doses of air into rabbits (usually 0.8 ml), we raised them to 4.5 km in a pressure chamber and kept them there for 5 min. At this altitude the intact rabbits showed no

essential functional changes except for a slight general inhibition and mild dyspnea. In rabbits which had been given air there were severe functional disorders after the ascent to altitude in the form of marked dyspnea, opisthotonos, loss of equilibrium, paresis of the limbs and even convulsions. These phenomena, undoubtedly associated with expansion of air emboli introduced into the blood vessels during the ascent, were more pronounced the shorter the interval between injection and ascent, and were absent when the interval was increased to 1 hr and 30 min — 1 hr and 45 min.

TABLE 2

Results of intravenous injection of air into rabbits after training for artificial air embolism

No. of animal	Subliminal dose of air (in ml) and duration of utilization	Doses of air administered after training (in ml)	Reactions to air administration and outcome of the experiment
1	0.6 ml daily for 6 days	2.5	Temporary general depression, transitory paresis of the hind legs. Survived
2	The same	2.5, and then 4.0	Dyspnea, temporary depression. Survived
3	0.6 ml daily for 6 days; 1.0 ml daily for 4 days; 1.5 ml daily for 5 days	2.0	The same
4	0.6 ml daily for 6 days 1.0 ml daily for 4 days; 2.0 ml daily for 5 days	4.0	Very transitory paresis of the hind legs. Survived
5	1.0 ml daily for 5 days	2.0	Marked dyspnea. Survived
6	0.6 ml daily for 6 days; 1.0 ml daily for 6 days; 1.5 ml daily for 3 days	2.0, and then 8.0	After administration of 2.0 ml, no persistent sequelae; after injection of 8.0 ml, flaccid paralysis of the hind legs. Survived
7	0.6 ml twice daily for 6 days; 0.8 ml twice daily for 6 days; 1.5 ml twice daily for 8 days	6.5 8.0	After first test, transitory paresis of the hind legs After second test, general paralysis of the whole body. Death
8	0.6 ml daily for 5 days; 0.8 ml daily for 6 days; 1.3 ml daily for 5 days	3.0	Marked dyspnea and general inhibition. Survived
9	0.6 ml three times daily for 5 days	4.0	General paralysis of the body. Death
10	0.6 ml three times daily for 5 days; 0.8 ml three times daily for 4 days	3.5	Transitory paresis of hind legs Survived
11	0.8 ml twice daily for 6 days; 0.6 ml three times daily for 5 days	4.5	Temporary paralysis of the hind legs and dyspnea. Survived

Rabbits raised to altitude at such periods after the injection of 0.8 ml of air were no different from intact rabbits. Hence, it may be concluded that during this period the body manages to cope with the dose administered, and at the time of the ascent the air emboli are completely, or mostly, eliminated. It is very interesting that the same rabbits, after many days' training with air injection, showed no functional disorders in the ascent to altitude even after considerably shorter intervals (45 min — 1 hr) between injection and ascent. Therefore, as a result of such training the body acquires the capacity of more rapidly eliminating air emboli injected into the blood.

Conclusion

Of all the phenomena produced by intravenous injection of air, the most striking is the predominant involvement of the hind legs and posterior half of the rabbits' bodies. Paresis and paralysis of the hind legs and the entire posterior half of the body are the most typical signs of severe artificial air embolism. It should be kept in mind that these symptoms are also found, as a rule, in severe decompression disorders. Paresis and paralysis of the lower half of the human body in caisson disease (the posterior half in animals) are usually thought to be the result either of gas formation in the actual spinal cord tissue or obstruction of the blood vessels of corresponding spinal segments by gas bubbles.

In our cases the first explanation is absolutely inapplicable; the second requires the assumption that the emboli pass through the pulmonary capillaries and obstruct the spinal cord blood vessels on the arterial side. However, this is also doubtful, because when air is injected into the veins it usually is not noted in the arteries (Gramenitskii and Savich, 1964). It remains for us to assume that the spinal cord functions suffer as a result of circulatory disorders and hypoxemia which develop at the same time. This explanation holds better for decompression paraparesis and paraplegia, since these phenomena are very constantly found with severe degrees of general anoxia, particularly in high-altitude hypoxemia.

As for the interpretation of the main fact found in long-term experiments (increase in resistance to intravenous injection of air), thus far we can only suppose the physiological mechanism underlying it. Undoubtedly, the main factor producing various reactions to artificial air embolism is obstruction of the pulmonary capillaries with gas bubbles. Evidently, reflexes can occur, first of all, from direct irritation of the capillary walls by the gas bubbles; secondly, from hemodynamic changes associated with obstruction of the pulmonary capillaries (increase of the pressure in the pulmonary capillaries and in the great veins of the greater circulation, and reduction of pressure in the pulmonary veins in the aortic system); and finally, from changes in the gas content of the arterial blood: as a result of obstruction of numerous pulmonary capillaries, it must be supposed that the gas exchange in the lungs is incomplete, i.e. hypoxemia and, perhaps, hypercapnia develop. In all three cases the reflexes must, evidently, be compensatory in nature; evidently, the training for air embolism which we noted is based on a perfected, better expressed occurrence of these

reflexes. Further studies should decide whether or not training for artificial air embolism will be useful in the body's fight against caisson disease during decompression from descent to depth and, conversely, whether the animals will show increased resistance to intravenous injections of gases after many repeated decompressions. The occurrence of such a crossed effect would prove the theory that perfection of protective reactions against air embolism underlies the increase in body resistance to decompression disorders.

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N66-17136

P. M. Gramenitskii and A. A. Savich

THE ROLE OF THE HYPOXEMIC FACTOR IN DEVELOPMENT OF DECOMPRESSION DISORDERS

(O roli gipoksemicheskogo faktora v razvitii dekompressionnykh rasstroistv)

An inadequate study has been made of the disturbance of gas transportation by the blood in the pathogenesis of decompression disorders associated with obstruction of pulmonary capillaries with indifferent gas bubbles. Various reports about gas exchange disorders in the development of signs of caisson disease appear in a number of papers (Hoppe-Seyler, 1857; Ber, 1878; Behnke, 1951).

As this problem is undoubtedly of practical as well as theoretical interest, we investigated the blood gases in animals exposed to the effect of increased pressure and subsequent decompression, and also to artificial air embolism.

Method

The experiments, short- and long-term, were conducted on dogs of both sexes, weighing 12 to 30 kg.

In performing the long-term experiments the animals, after an ordinary walk, were placed in a two-compartment compression chamber under pressures of 1.6 and 2.0 atm for 4 hrs, or under a pressure of 4.5 atm for 35, 40, 45 and 50 min, after which decompression was performed at a rate of 10 m/min.

Arterial blood was taken from the femoral artery by cardiac puncture before the dog was placed in the chamber (control) and at various periods under decompression. This blood was put into a test tube under vaseline oil. Samples of blood taken from dogs during periods of preparation for the experiments and adaptation to needle punctures served as controls.

The following procedure was used for the short-term experiments. Under morphine-hexenal anesthesia and after tracheotomy, with the blood vessels prepared beforehand for recording the blood pressure and taking blood, the dogs were placed in a compression chamber at pressures of 5.0 and 7.0 atm long enough for overt decompression disorders to develop as a result of subsequent rapid decompression. After decompression at 10 m/min, the respiratory movements, blood pressure and taking of the blood samples from the femoral artery were recorded on a kymograph. To observe gas formation in the venous blood, gas traps were used in a number of experiments (Gramenitskii and Savich, 1963). Gas composition of the blood was analyzed on a van Slyke apparatus.

As we have given a detailed description of the graded injection of gases in an appropriate paper (Gramenitskii, Savich, and Yurova, 1964), we shall not dwell here on the method of performing experiments associated with investigation of blood gases in artificial air embolism. In all, we performed 14 long-term and 6 short-term experiments, not counting preparatory experiments with investigation of gas content of the blood under ordinary conditions.

Results of the Experiments and Discussion

In long-term experiments, the oxygen and carbon dioxide content in the arterial blood of experimental dogs not exposed to the effects of increased pressure varied within physiological limits. The dog Druzhok differed somewhat from the other animals, in that its blood had a comparatively low oxygen content and high carbon dioxide content.

Change in the gas content of the arterial blood in dogs with development of signs of caisson disease

Name of the animal	Depth (in m)	Exposure time (in min)	Time after decompression (in min)	Appearance of symptoms of the "bends" type	Arterial blood gases (in volumes %)			
					Initial background		After the effect	
					O_2	CO_2	O_2	CO_2
Sedoi	45	50	10	Overt	22.05	39.93	21.56	41.26
Zor'ka	45	50	10	The same	24.09	41.20	23.85	39.32
Druzhok	45	40	17	Very severe	15.00	44.96	7.86	52.43
	45	35	19	Absent	16.42	44.96	13.48	46.05
Mishka	45	45	19	Overt	21.81	35.40	15.93	43.90
Sedoi	45	45	10	Very severe	22.21	39.81	13.57	45.46
	16	240	80	Absent	21.47	37.39	21.71	39.27
Zor'ka	24	240	23	The same*	23.43	37.39	21.47	39.81
Mishka	16	240	23	"	19.74	38.09	15.25	39.27
Druzhok	45	40	25	"	15.71	44.92	13.82	47.08
			60	"			11.82	46.54
			101	"			20.48	41.43
	20	300	35	"	15.8	44.7	13.86	45.54
			60	"			18.97	39.51
Sedoi	20	240	30	"	21.9	38.6	20.05	39.2

* A subsequent ascent to altitude revealed the presence of a "latent" bubble.

After decompression, both in the case of overt symptoms of caisson sickness of the "bends" type and in the absence of visible functional disorders in the limbs, hypoxemia was noted in all the animals. The

degree of development of hypoxemia was directly related to the severity of the experimental animal's condition (see table).

From the data presented in the table it is evident that the development of pronounced decompression disorders of the "bends" type is always associated with a reduction of the oxygen content in the arterial blood; the more marked the joint symptoms, the greater the degree of hypoxemia which occurs.

Almost always, a reduction of the oxygen content in the blood is associated with an increase of carbon dioxide content, which at times reaches high figures.

Neither hypoxemia nor hypercapnia, which occurs in cases of pronounced decompression disorders, appears to us unusual or unexpected. Undoubtedly, in such cases more or less active gas formation always occurs in venous blood. Naturally, disorders of gas exchange between alveolar air and blood must be a direct result of obstruction of the pulmonary capillaries with bubbles of the indifferent gas.

The most interesting facts obtained are those indicating the development of distinct hypoxemia in those cases where there are no joint symptoms in the dogs after they emerge from increased pressure, and the reaction to decompression is manifested only as scratching, dyspnea, and some depression. Such signs may be extremely slight, and sometimes they do not occur at all. This was shown with particular distinctness in experiments on the dog Druzhok. In this dog, the oxygen content of the blood fell 3—4 volumes %, as the table shows, without even initial signs of functional disorders in the limbs. Repeated determinations of the gas content of the blood in one experiment showed that sometimes in the absence of decompression symptoms hypoxemia progresses for an hour after decompression (experiment 10), but eventually, in one way or another, the quantity of oxygen in the blood increases and even exceeds the original figures.

All this data indicates that following decompression from increased pressure, gas formation in the venous blood occurs not only in cases of distinct disorders of the "bends" type. Even in their complete absence, a quantity of gas bubbles evidently may be formed in the venous blood which, by blocking the pulmonary capillaries, causes hypoxemia and hypercapnia. The fact that a reduction of the oxygen content in the arterial blood is associated with signs of decompression disorders rather than with some other factors has been confirmed by experiments in which ascent of the animals to altitude after the blood has been taken was associated with the immediate development of typical decompression symptoms of the "bends" type.

Study of the gas content of the arterial blood in short-term experiments during the development of decompression disorders as well as in experiments with artificial air embolism confirmed the data presented above and the conclusion stemming therefrom.

As the experiments showed, pronounced hypoxemia occurs both in caisson sickness caused by decompression and the intravenous injection of air.

A reduction of the blood oxygen in decompression and artificial air embolism is observed even when no appreciable disorders are seen in respiratory or cardiovascular activity; it progresses with the appearance of and increase in these disorders, and in case of critical disorders

Changes in the respiration and gas content of blood of an anesthetized dog after the intravenous injection of air

a — respiration; b — blood pressure; c — time marking, 1-second intervals (the baseline of the blood pressure). 1 — initial background; 2 — 10 min after the injection of 50 ml of air in 30 sec; 3 — 2 min after the 2nd injection: 200 ml of air in 2 min and 30 sec; 4 — 2 min after the 3rd injection: 150 ml of air in 1 min; 5 — 17 min after the last injection; 6 — 42 min after the last injection.

reaches figures so low as to be incompatible with life. In the case of decompression air embolism, the reduction of the oxygen content in the blood is directly related to the intensity of gas formation in the veins; in artificial air embolism, to the quantity of air injected intravenously.

In those cases where the animal does not die of air embolism and normalization of respiration and circulation occurs the oxygen content of the arterial blood increases considerably.

Data of one of the experiments with artificial air embolism, represented on the figure, shows distinctly the relationship between changes in the gas content of the blood and the intensity of air embolism, and the interrelationship of these changes and respiratory and circulatory reactions. This serves as a striking illustration of the regularities noted, and also confirms once again the great capacity of the body for eliminating air emboli which enter the pulmonary blood vessels. It is only by such elimination that the blood oxygen content which has fallen sharply after the third administration of air could subsequently begin to increase steadily.

The overall results lead us to conclude that changes in the gas content of the arterial blood occur as a constant phenomenon in decompression air embolism. They also pose the question of the significance of these changes in the oxygen and carbon dioxide content of the blood (and evidently also their tensions) for the organism which has been exposed to decompression disorders. It is very likely that hypoxemia, which in itself does undoubted harm to the body, is of benefit in these cases if it does not reach

excessive degrees, because it contributes to activating the respiration and circulation, thereby contributing to elimination of air emboli from the lungs.

In conclusion, it is important to emphasize once again that reduction of the oxygen content is found with the first signs of caisson sickness (a very slight general depression, barely noticeable change in respiration) and precedes the development of typical decompression symptoms of the "bends" type. Hence, we need to investigate blood oxygenation in divers and caisson workers exposed to decompression and after being under increased pressure. The possibility has not been ruled out that oximetry would be useful for the early diagnosis of decompression disorders.

Conclusions

1. The development of severe forms of decompression disorders is always accompanied by a pronounced hypoxemia and hypercapnia.
2. Reduction of the oxygen content of the arterial blood in animals exposed to subliminal increased pressures occurs, as a rule, in the absence of typical decompression symptoms.
3. Hypoxemia and hypercapnia are the results of air embolism in capillaries of the lesser circulation.
4. Changes in the gas content (oxygen and carbon dioxide) of the arterial blood are an inseparable component of the body's reaction to decompression.

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V. A. Aver'yanov and K. S. Yurova

EXPERIMENTAL AIR EMBOLISM UNDER CONDITIONS OF HYPO- AND HYPERTHERMIA

(Eksperimental'naya aeroemboliya v usloviyakh gipo- i gipertermii)

Two facts constituted the basis of the present study, directed at a physiological analysis of decompression disorders. The first is the essential role of air embolism in the pathogenesis of decompression disorders. From the investigation of A. P. Brestkin (1952), I. I. Vavilov, and P. M. Gramenitskii (1958), P. M. Gramenitskii, A. A. Savich and K. S. Yurova (1963) it follows that in decompression, gas formation occurs most readily in blood coming from tissues supersaturated with an indifferent gas, and that the air embolic process beginning in the venous capillaries and ending in obstruction of pulmonary capillaries is the main phenomenon in decompression disorders. The second fact was the indisputable effect of temperature conditions on the occurrence of decompression disorders, which stems both from practical observations and from the few existing experimental investigations (Brestkin, Gramenitskii, Oblapenko, 1958).

Both of these facts naturally led to the question of how altered temperature conditions would affect the development of air embolism and the resistance of the body to its deleterious influence. The present investigation deals with this question.

Method

The experiments were performed on rabbits of both sexes weighing 1.9 to 4.0 kg. In all, 23 long-term and 18 short-term experiments were performed.

In the long-term experiments 2 ml of air were injected into the auricular veins of the rabbits in 1 minute; afterwards the animals remained free, and their reactions to the given effect and the outcome of air embolism were observed. Of 23 rabbits, eight served as controls and were not exposed to any effects before the air administration; eight were exposed to preliminary cooling and seven to preliminary overheating.

In the short-term experiments the control, overheated and cooled rabbits were in a fixed position without anesthesia; their blood pressure and respiration were recorded by the usual means on a kymograph. These animals were given injections of 1 ml of air in a period of 30 sec every

20 min until they died; the circulatory and respiratory reactions to the separate injections of air were compared, and a record was made of the total number of injections given.

The animals were cooled by putting them in a Nikolaev-Subbotin tray (a metal container with double walls shaped to the rabbit's body), which was filled with water and chopped ice.

In the long-term experiments, when the rectal temperature had dropped to 34.4—34.0°, (which took 1—2 hrs), the animals were taken out of the tray and immediately injected with air. In the short-term experiments the rabbits were left in the tray in the fixed position throughout the experiment. When the rectal temperature dropped to 34°, cold water and ice in the tray were replaced by warmer water (20—25°) so that the animal's temperature could be maintained at the same level as far as possible.

The rabbits were overheated in both the short-term and long-term experiments by means of a special wooden box with a little door and an observation window. Seven electric light bulbs inside the box maintained the air temperature at 42—43°. After the rectal temperature had risen to 42° the animal was taken out of the box and immediately injected with air in the long-term experiments, just as in the case of hypothermia. In short-term experiments, after the rectal temperature had gone up to 41.6—42.0°, the animals were taken out of the box and put into a Nikolaev-Subbotin tray filled with hot water (43—44°). In those cases where the rectal temperature of the animals in the tray began to drop they were covered with hot water bottles. The rectal temperatures were measured with a thermocouple and a maximum thermometer until the onset of heating (or cooling) and then throughout the experiment.

Results of Long-Term Experiments

Of the eight control rabbits, two, heavier than the rest (3.5—3.8 kg), were able to tolerate the injection of 2 ml of air; the other six died. Death of the animals occurred in the first 7 min after the injection of air; it was preceded by paralysis of the hind legs and generalized convulsions (Figure 1).

Of the eight cooled rabbits which had been injected with the same quantity of air as the control group only two died. In the cooled rabbits, in contrast to the controls, after the injection of air there was more pronounced dyspnea; the general depression and motor disorders (change in muscle tone and in position) were less pronounced (Figure 2).

The period of complete functional recovery in the surviving cooled rabbits lasted more than two hours, and was longer than that of the surviving controls. Probably, this was connected with the extremely slow recovery of the rectal temperature of the cooled rabbits because of marked dyspnea increasing the heat output. Therefore, the cooled rabbits were more resistant to air embolism.

The overheated rabbits tolerated the injection of 2 ml of air better than the controls but not quite so well as the cooled animals. Of the seven overheated rabbits, 3 died. In the overheated animals, following the injection of air a marked general depression occurred, and persistent opisthotonus developed (Figure 3); tachypnea caused by overheating

increased further, whereby respiration became deeper and involved participation of the abdominal muscles. The general condition of the surviving animals became normal at the end of the second hour after air injection.

Therefore, overheating, and, particularly, cooling of the rabbits increased their resistance to artificial air embolism.

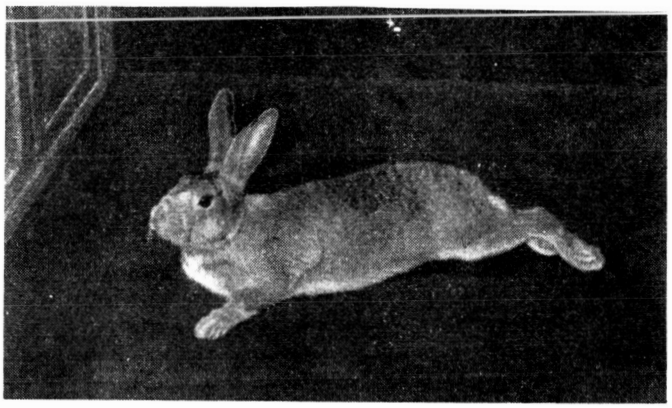


FIGURE 1. Rabbit No. 20. Experiment of 10 March 1960. General condition of the control rabbit in the 3rd minute after intravenous injection of 2 ml of air (paresis of the hind legs)

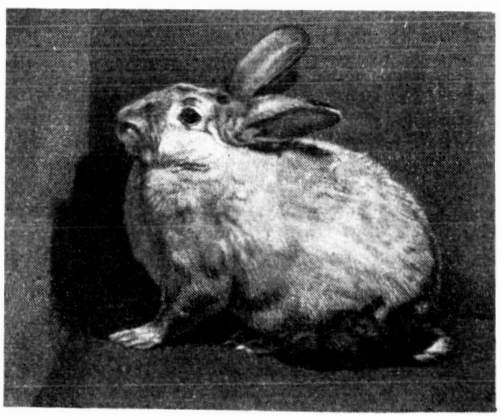


FIGURE 2. Rabbit No. 30. Experiment of 11 April 1960. General condition of cooled rabbit in the 5th minute after intravenous injection of 2 ml of air

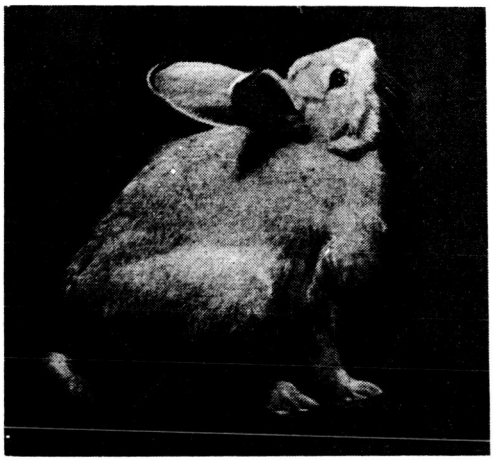


FIGURE 3. Rabbit No. 31. Experiment of 12 April 1960. General condition of overheated rabbit in the 5th minute after intravenous injection of 2 ml of air

Results of Short- Term Experiments

Typical changes in the respiration and blood pressure occurring after intravenous injection of 1 ml of air in five control rabbits are shown in Figure 4. In these animals, following the first injection of 1 ml of air, a considerable depressor effect with pronounced bradycardia was immediately noted. After 1.5—2 min the blood pressure dropped 32—53% below the original figure, which was 110—120 mm Hg. The heart rate slowed from 110—130 to 50—75 beats a minute. On the blood pressure curve tertiary waves appeared in all cases; dyspnea occurred immediately.

All the control rabbits died after one or two injections of air, except for one, which was able to tolerate three injections.

In the seven [sic] cooled rabbits the initial blood pressure level was somewhat higher; the pulse rate somewhat slower, and respiration deeper than in the control animals. The cooled rabbits reacted to the initial injection of air with a more gradual and less pronounced blood pressure reduction (Figure 5). Dyspnea also developed more gradually and reached a maximum with the appearance of pronounced bradycardia in the 4—6th minute after injection of air. Resistance of the cooled rabbits to the air embolism was much greater than that of control animals even in these experiments: they died after only 4—5 air injections.

Overheating of the rabbits (6 animals) [sic] lowered the pressure somewhat and caused a considerable increase in the respiratory and cardiac rates. The reactions of the overheated animals to the air injection were somewhat unusual. Instead of the depressor effect, initially a general rise in the blood pressure was noted with marked tertiary waves and a distinct vagal pulse (Figure 6). Respiration, superficial and as fast as possible before the injection of air, became somewhat shallower and slower after it.

The overheated rabbits also were more resistant to air embolism than the controls. They tolerated 2—3 air injections. It is significant that

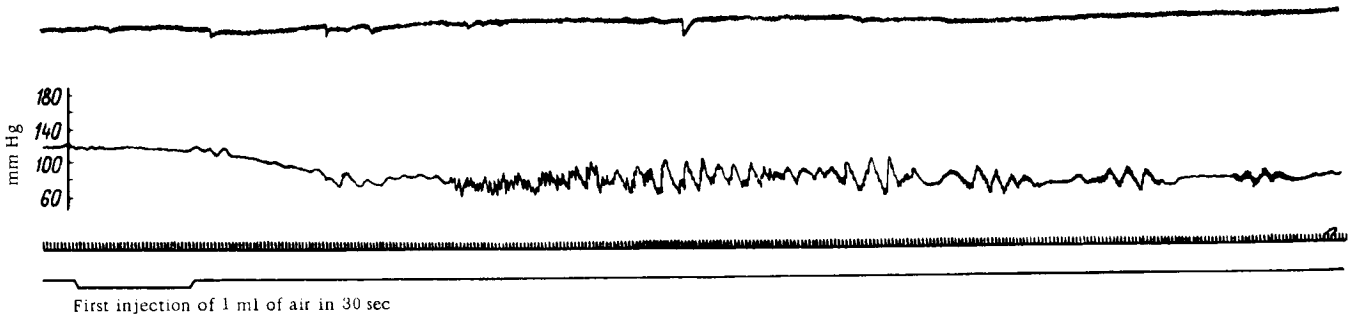


FIGURE 4. Experiment of 20 April 1960. Reaction of control rabbit to intravenous injection of air

From above down: respiration, blood pressure, time marking (one-second intervals), marking of air injection. The figures on the second curve represent the blood pressure in mm Hg

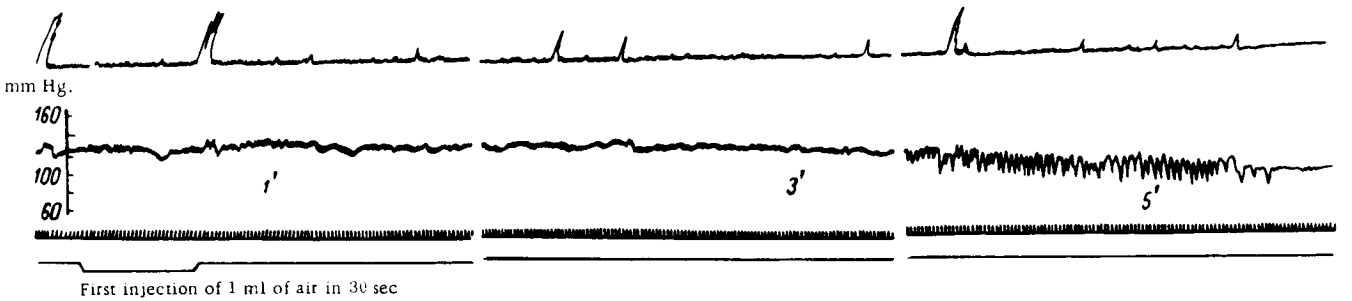


FIGURE 5. Experiment of 22 April 1960. Reaction of cooled rabbit to intravenous injection of air

The key is the same as in Figure 4.

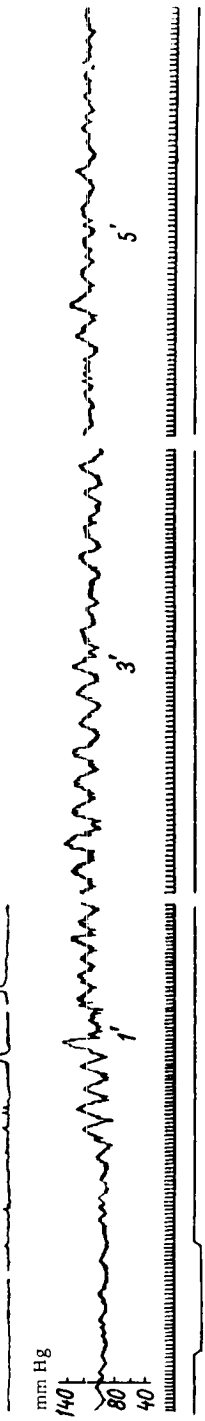


FIGURE 6. Experiment of 23 April 1960. Reaction of overheated rabbit to intravenous air injection

The key is the same as in Figure 4.

their deaths occurred suddenly; the blood pressure suddenly began to drop sharply from quite a high level; marked respiratory disorders appeared, and death occurred. The short-term experiments showed, therefore, that both the overheated and particularly the cooled rabbits tolerated a larger number of air injections than the controls. These results generally coincided with those of long-term experiments

Discussion of Results

The experiments conducted showed, first of all, an increase in the resistance of overheated and particularly cooled animals to air embolism; secondly, some changes in the reactions of the body in a state of hyper- or hypothermia to intravenous air injection. The question arises as to the basis of the increased body resistance to air embolism under the influence of overheating and cooling. Overheating causes tachypnea, accompanied by increase in pulmonary ventilation, increases the cardiac rate, and the general blood flow. All these reactions are undoubtedly useful to the body in its fight against air embolism; they contribute to fractionation of air bubbles passing through the heart, and to the most rapid elimination of air emboli obstructing the pulmonary capillaries. However, the situation evidently did not amount to these positive factors. Intravenous air injection into overheated animals not only failed to reduce their typical depressor reaction, but caused an unusual pressor effect with undulating blood pressure variations and after a number of air injections, sudden death. It may be assumed that this is connected with dilatation of pulmonary capillaries under the influence of

overheating and with penetration of air emboli into the greater circulation and cerebral blood vessels. The probability of such an assumption has been confirmed by the data of P. M. Gramenitskii and A. A. Savich (1964), who, in experiments with gas traps, recorded the same reactions with a considerable number of gas bubbles in the arterial blood.

According to the data of a number of authors (Val'ter, 1866; Egorov, 1956; Metelitsa, 1956), in the initial period cooling also leads to an increase in pulmonary ventilation, acceleration of the blood flow and increase in blood pressure. The latter has also been confirmed by short-term experiments performed by us. Therefore, with certain degrees of cooling favorable conditions are created for the elimination of air emboli injected into the venous blood. However, a considerable increase in the resistance of the cooled organism to intravenous air injection is evidently based not only on the reactions mentioned. Air embolism of pulmonary vessels undoubtedly causes, along with protective compensatory reactions, a number of unfavorable reflexes. Among them may be mentioned, for example, reduction of blood pressure in the greater circulation with increase in the pressure in the pulmonary arteries (Schwiege, 1935; Parin, 1939).

Air embolism is, in addition, accompanied by such consequences as hypoxemia, which has an unfavorable influence chiefly on the central nervous system. Hypothermia of the body exerts an inhibitory effect on the central nervous system (Tsynkalovskii and Azhipa, 1956), and thereby reduces its sensitivity to unfavorable reflexes and direct influences. Evidently, this explains why increase in body resistance to artificial air embolism is greater with cooling than with overheating.

In conclusion, it is essential to compare the facts we have obtained with data concerning the effect of cooling and heating of the body on the occurrence of decompression disorders. As has been determined by V. A. Aver'yanov (1962), heating of the body during nitrogen desaturation prevents the development of decompression disorders; cooling under the same conditions increases the frequency with which they occur. In his experiments the temperature factor acted on animals whose bodies had been supersaturated with nitrogen: heat accelerated the process of tissue desaturation and reduced or prevented the formation of gas bubbles in the blood flowing out of them; cold acted in the opposite way. In other words, the entire situation amounted essentially to a change in the nitrogen desaturation rate under the influence of temperature changes. In our experiments there was no supersaturation of the body with an indifferent gas, and the entire situation amounted to the body's control of artificially created air embolism. The data obtained by V. A. Aver'yanov and the results of our experiments are not contradictory.

Conclusions

1. In overcooling and overheating of rabbits there is an increase in their resistance to artificial air embolism. This increase is more pronounced in hypothermia than in hyperthermia.

2. The mechanisms of increase in resistance to air embolism in hypo- and hyperthermia are apparently somewhat different. In hyperthermia

they consist chiefly of reactions which contribute to a more rapid removal of air bubbles from the blood stream. In hypothermia, along with side reactions, reduced sensitivity of the central nervous system to unfavorable reflex influences caused by gas bubbles and to hypoxemia accompanied by air embolism is of great importance.

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V.T. Arsen'eva, P. M. Gramenitskii, and K. S. Yurova

COMPARATIVE CHARACTERISTICS OF RESPIRATORY AND CIRCULATORY REACTIONS OF UNANESTHETIZED DOGS TO DECOMPRESSION AND ARTIFICIAL AIR EMBOLISM

(Sravnitel'naya kharakteristika reaktsii dykhaniya i krovoobrashcheniya nenarkotizirovannykh sobak na dekompressionnuyu i iskusstvennuyu aeroemboliyu)

From a number of papers dealing with physiological analysis of caisson sickness (Brestkin, 1958; Vavilov and Gramenitskii, 1958; Gramenitskii, Savich, and Yurova, 1964), it follows that air embolism in the venous system and pulmonary capillaries plays the leading part in the mechanism of development of decompression disorders. These works also study respiratory and circulatory reactions of various animals to decompression and artificial (produced by intravenous air injection) air embolism in short-term experiments, and the similarity in principle between these reactions is shown in various cases.

The experiments of Gramenitskii and Yurova (1964) with repeated intravenous injections of air into rabbits demonstrated the possibility of training the body for artificial air embolism. A comparison of this fact with previous data suggests the likelihood that the increase in body resistance to frequently repeated decompression effects (Aver'yanov, Gramenitskii and Savich, 1961) is also based on training of the body for air embolic phenomena. The present investigation was made in order to check this supposition and to definitively substantiate conclusions of previous work. The first task was to study respiratory and cardiovascular reactions of unanesthetized animals to decompression and artificial air embolism in frequently repeated long-term experiments. The second task was determining whether training for artificial air embolism is effective with respect to decompression, and, conversely, whether increased resistance to the decompression effect results in increased resistance to intravenous injection of several gases simultaneously.

Method

The experiments were performed on three dogs with carotid arteries exteriorized in a skin flap. The animals were trained to lie quietly on one side in a special cage in a fixative suit and to breathe through a mask. Respiration and pulse were recorded by carbon pickups on an MPO-2

oscillograph, pulmonary ventilation by a gas meter furnished with electric contacts, the electrocardiogram was recorded with three standard leads. A record of these indices in some cases was made immediately after rapid decompression from 4.5 atm (exposure 15—60 min); in other cases, after intravenous injection of air (in a quantity from 20 to 50 ml in 1—2 min).

A special system was used for injecting air. The apparatus is shown in Figure 1. A glass ball (a) having two outlets was connected by rubber tubes in its lower portion to a graduated burette (b) and in its upper part, to the bag of ISAM- 48 apparatus (c). In this bag, through a reducer (d) connected to the tank, an increased air pressure was created. It was used first to drive the water in the system out of the burette into the ball and then, experimentally to displace the water from the ball into the burette. Thereby the air found in the burette entered the rubber tube connected to its upper end and then, through a thin injection needle (e) inserted into the animal's vein, entered the blood. In experiments with decompression, when the dogs developed the typical signs of caisson sickness in the limbs the record was continued for 3—5 min, and then a therapeutic recompression was performed. In all, 187 experiments with decompression of the animals from increased pressure and 44 experiments with intravenous injection of gases were performed.

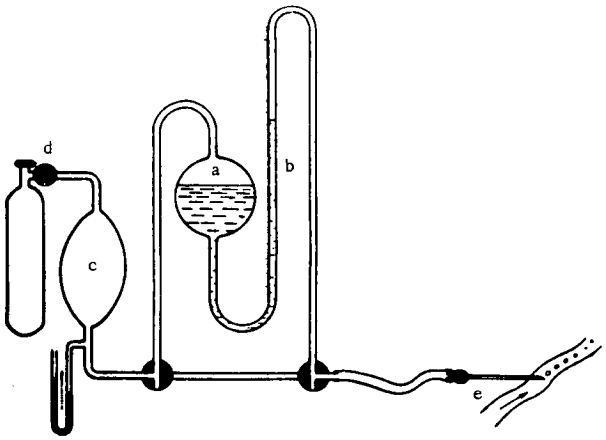


FIGURE 1. System for intravenous injection of air

Explanation in the text.

Results of Experiments and Discussion

The experiments showed that changes in respiration and cardiac activity in intact animals under the effect of decompression and intravenous air injection are very similar. In both cases dyspnea always occurs with greater or lesser increase in pulmonary ventilation, and, as a rule, the

pulse slows. In initial experiments where adaptation has not yet been created to corresponding effects, the intensity of the dyspnea and bradycardia during decompression depends directly on the duration of exposure of the animals under pressure; after air injection, on the dose and rate of injection. It is significant that the changes noted in respiration and cardiac activity during decompression occur not only in those experiments which terminate in development of typical symptoms in the limbs, but also in those which are not associated with these symptoms and, in view of the brevity of the exposure time "at ground level," do not even threaten to develop.

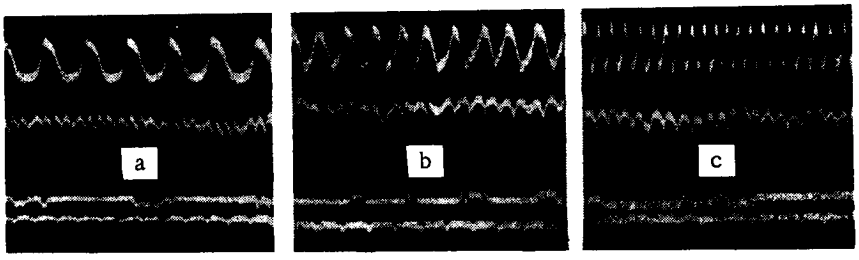


FIGURE 2. Changes in respiration, pulse and pulmonary ventilation in the dog Volchok after decompression from 4.5 atm (exposure of 6 min)

From top down: respiration, pulse, pulmonary ventilation (200 ml marking); time marking, 1-second intervals: a — 10 min; b — 20 min; c — 30 min after completion of decompression.

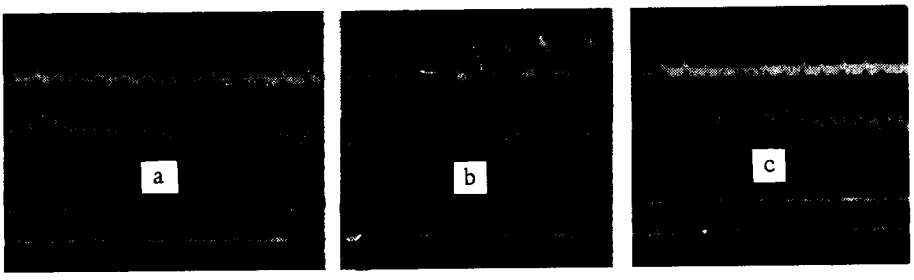


FIGURE 3. Changes in respiration, pulse, and pulmonary ventilation in the dog Kudryash during the development of typical decompression symptoms (pressure 4.5 atm, exposure 20 min)

a — 10 min; b — 30 min; c — 40 min after decompression (occurrence of symptoms). The rest of the key is the same as in Figure 2.

Along with a general similarity in the reactions to decompression effects and intravenous injections of air, there are also certain differences, primarily with regard to the dynamics of change of respiration and cardiac activity. In artificial air embolism, dyspnea and slowing of the heart rate are most pronounced in the first 5—10 min after the injection of air; then they gradually slacken and in a number of cases, at the end of the experiment,

after 50 minutes, they disappear entirely. After decompression dyspnea and bradycardia develop gradually, reaching a maximum in the 20th—30th minute in experiments which are not associated with joint symptoms; in experiments where joint symptoms do occur later, dyspnea and bradycardia progress up to the point where such symptoms make their appearance. This fact becomes perfectly understandable if we consider that air embolic

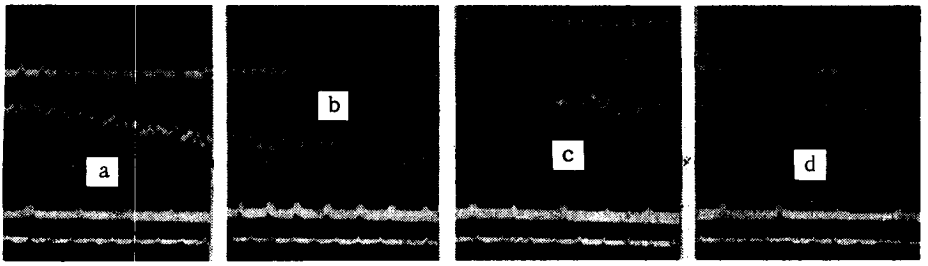


FIGURE 4. Changes in respiration, pulse, and pulmonary ventilation in the dog Volchok after intravenous injection of 50 ml of air in 2 min and 15 sec

a — before injection; b — at the end of the injection; c — after 10 min; d — after 20 min. The rest of the key is the same as for Figure 2.

phenomena caused by decompression develop gradually, and at the depth and exposure times which were used in the experiments they most frequently reach a maximum specifically 20—30 min after emerging from under pressure. A characteristic of the reactions studied in the case of artificial air embolism is the brief tachycardia during the course of the air injection, which is immediately replaced by bradycardia at the end of the injection. In cases of decompression effects, these reactions acquire their characteristic features during the development of symptoms in the limbs. When these symptoms do occur bradycardia is then replaced by an increase in the pulse rate, and respiration becomes more frequent but more superficial, and the dogs show motor restlessness. All this is evidently explained by the occurrence of severe pain in the affected limb.

In Figure 2 an experiment is shown with decompression effects taking place without typical symptoms in the limbs but accompanied by a pronounced general depression of the dog, noticeable even at the end of the record with the animal in a natural position. The figure shows an increase in dyspnea during the course of the experiment and the development of bradycardia in the 20th minute after decompression. In Figure 3 a case is shown with painful symptoms occurring 38—40 min after decompression. From the oscillograms it is evident that a marked bradycardia (record taken in the 30th minute) is replaced by a relative increase in the pulse rate; respiration became more frequent but more superficial. In Figure 4 an experiment is shown with the intravenous injection of air. The oscillograms illustrate the tachycardia at the end of the air injection, which is replaced by a slowing of the pulse and dyspnea, most pronounced on the record made 10 min after the injection.

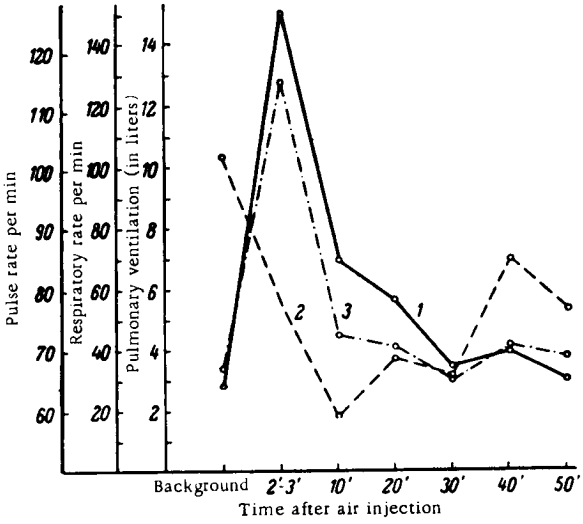


FIGURE 5. Typical changes in the respiration pulse and pulmonary ventilation after intravenous air injection (experiment of 13 October 1961; the dog Volchok, injected with 50 ml of air in 2 min and 15 sec)

1. Respiratory rate; 2. pulse rate; 3. pulmonary ventilation in 1 min.

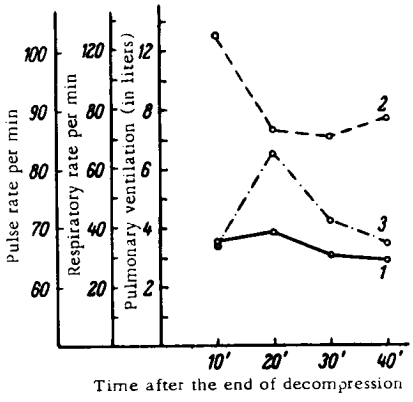


FIGURE 6. Typical changes in the pulse, respiration, and pulmonary ventilation in decompression (experiment of 22 May 1961; the dog Volchok; pressure of 4.5 atm; exposure 50 min)

The key is the same as for Figure 5.

In Figures 5 and 6 graphs are shown which represent the typical dynamics and scales of the functional changes studied during artificial and decompression air embolism. It should be noted that the absence of essential changes in the respiratory rate in decompression experiments does not signify the absence of dyspnea. In these cases it developed essentially because of the increased amplitude of respiratory movements rather than because of the rate.

The main changes in the electrocardiograms, both in the case of decompression and artificial air embolism, amount to the following. First of all, a shift to the right of the cardiac axis is found. This is evidenced by the index R_{III}/R_I, which reflects the ratio of the heights (voltages) of the corresponding waves. In the control experiments this index was equal, on the average, to 1.7 with variations from 0.7 to 3.7 for different experiments and different dogs. After decompression and particularly after an injection it usually increased considerably, and in a number of cases was found equal to 5, 5.5 or even 6. It must be supposed that the right axis deviation in these cases reflects an increased functional load on the right ventricle of the heart associated with an obstruction of the pulmonary capillaries by air emboli.

The second typical ECG change was the inversion at the beginning of the T wave, which was particularly noticeable in the second lead. While normally negative, T_2 becomes positive or biphasic in air embolism. This undoubtedly serious change in the ECG is reflected in Figure 7, where at the same time a marked bradycardia and arrhythmia are readily seen in this case after the injection of air.

In agreement with previous data, the experiments performed showed that after frequent repetition of the effects there is a considerable increase in the animal's resistance both to the intravenous air injection and to decompression.

Increase in resistance to artificial air embolism after regularly repeated effects was manifested in the dogs' ability to tolerate doses of air twice as great as the original with no greater discomfort. Thus, judging from external appearance, the general condition and the rapidity with which respiration and cardiac activity became normal, the dogs tolerated the injections of 45—50 ml of air after repeated experiments with artificial air embolism in the same way as they had initially tolerated it in a dose of 20—25 ml.

Increased resistance of the animals to decompression effects during the course of the experiments was evidenced by a considerable increase in the safe time they were at a depth of 45 m, determined by the occurrence of typical post-decompression signs in the limbs. Thus, in the dog Volchok this time increased from 40 to 60 min; true enough, following a persistent hind leg paresis which was eliminated after a month it again decreased to 50 minutes. In the dog Timoshka the safe period increased from 25—40 min; in the dog Kudryash, 15—40 min.

It is most significant that in experiments with two dogs, increased body resistance to the effect of decompression was accompanied by a simultaneous increased resistance to artificial air embolism, and vice versa. In the first dog (Kudryash) regular experiments with the effect of decompression were conducted for several months. During this time the reaction of the animal to air injections given every two weeks was checked. It was found that these trial injections of air were tolerated progressively better by the animals, although we cannot in any way suppose that the animal had been adapted by training to the actual air injections.

The second dog (Volchok) was first exposed to repeated decompression effects. At the beginning of these experiments, the maximum safe time on the "bottom" was 40 min; at the end of the experiments, 50 min. Then for a month the animal was intravenously injected with air 22 times. A check on the safe time after this showed that it had increased to 65 min. Therefore,



FIGURE 7. Development of bradycardia and inversion of T_2 of the ECG in the dog Volchok after intravenous injection of 44 ml of air in 50 sec All the ECG's were recorded with the second lead; a — before the air injection; b — 2 min after; c — 10 min after; d — 20 min after injection.

training for artificial air embolism led to an additional increase in resistance, greater than achieved by repeated decompression effects.

The cross-training effect found left no doubt that increase in the body's resistance to repeated decompression effects is based, to a considerable degree, on the perfection of reactions produced by air embolism. The experiments actually showed that with repetition of the effects of decompression and intravenous air injection, the respiratory and cardiovascular reactions were somewhat modified.

Bradycardia is progressively less pronounced, in various cases does not occur at all and is even replaced by increase in the heart rate. Dyspnea persists, although it becomes somewhat more moderate during the repetition of the experiments. The inversion of the ECG waves mentioned decreases and disappears; the right axis deviation persists. Finally, it is significant that with repetition of the experiments dyspnea and tachycardia occur by conditioned reflex in the animals from the experimental situation alone and from conditioned stimuli associated with air embolism (placement in the cage, bubbling of the air through the water valve of the system for gas injection, noise of the tape-winding mechanism of the oscillograph).

Therefore the reactions to decompression and artificial air embolism are perfected, first of all, in that components unfavorable to the body disappear and there is an increase in the protective functional changes; secondly, in that these reactions, which previously were more complete, are initated sooner, even prior to the appearance of gas bubbles in the blood.

Conclusions

1. Changes in respiration and cardiac activity which occur in unanesthetized dogs during decompression and artificial air embolism are similar in principle.
2. Training the organism for artificial air embolism increases its resistance to the effects of decompression; likewise, training for decompression effects increases resistance to intravenous gas injection.
3. Increased body resistance to decompression effects when they are repeated frequently is based, to a considerable degree, on the perfection of respiratory and cardiovascular reactions produced by air embolism.

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V. A. Livshits

SIMPLE "CALCULATED TISSUE" MODELS

(Prostye modeli "raschetnoi tkani")

The saturation processes of various body tissues with an indifferent gas have not been studied experimentally. Haldane's suggested equation (Boycott, Damant, and Haldane, 1908), expressing the rate at which gaseous and solid substances dissolve in liquids under conditions of ideal mixing, when the concentration in the fluid becomes uniform exceedingly rapidly, has been used to date in the calculation of decompression conditions (Shchukarev, 1896; Donnan and Masson, 1920; Belopol'skii, 1946; Pozin, 1946; Kishenevskii and Pamfilov, 1949; Nichik, 1949; Turkhan, 1950; Brestkin, 1952). This equation is as follows:

$$\frac{dp}{dt} = \frac{1}{\tau}(p_a - p), \tag{1}$$

where p is the tension of the dissolved gas in the solution;
t is the time;
$1/\tau$ is a constant characterizing the rate at which the given gas dissolves in a given fluid;
P_a is the partial pressure of the dissolved gas;
$P_a = \frac{P_n}{100}$, where n is the percentage of the given gas in the mixture.

According to Haldane, the process of saturation of the body with indifferent gases occurs schematically in the following way. The organism is a kind of combination of "calculated tissues" which do not react with one another and which differ with respect to the rate at which they are saturated with gas. The blood circulates between the lungs and the "calculated tissues," exchanging gases in each place. In a simplified form it is believed that the blood manages to go into complete gaseous equilibrium both with the "calculated tissue" and the gas in the lungs. If, in addition, we consider only the time intervals which are long in comparison with the time the blood moves from the lungs to the "calculated tissue," the exchange of gas between the lungs and the tissue may be represented schematically by the process of solution of the gas in the fluid (simulating tissue) after direct contact between them. The schema adopted by Haldane permits using a differential equation (1) in every calculated tissue.

Therefore, equation (1) says that the rate of tissue saturation is directly proportional to the difference between the partial pressure of the gas in the lungs and its tension in the tissues.

If in equation (1) we consider P_a constant, by simple integration we obtain the usual Haldane exponential equation from equation (1)

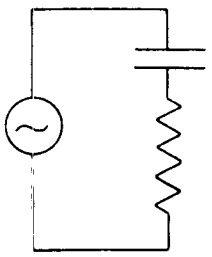
$$P = P_a - (P_a - P_0) \cdot 0.5^{\frac{t}{\tau}}, \tag{2}$$

where $P_0 = P/t=o$.

The latter is unsuitable for calculating conditions in those cases where the external pressure does not change suddenly, but steadily. However, equation (1) is suitable not only for a constant but also for variable P_a. In this form equation (1) represents a generalization of the usual exponential equation.

At the request and with the direct participation of G. A. Zarakovskii we, on the basis of equation (1), worked out a method of calculating continuous decompression conditions (smooth reduction of pressure used in decompression of caisson workers as well as in treatment of caisson sickness). An analysis was made of the conditions under which the permissible supersaturation coefficient (ratio of gas tension in the "leading" tissue to the total pressure) or the degree of permissible supersaturation (difference between gas tension in the "leading" tissue and the total pressure), remains constant. By the method we devised, Zarakovskii calculated some specific conditions.

Equation (1) is the same as the equation for the voltage at the capacitor of an RC-circuit (R is a resistor and C is a capacitor), connected to a source of emf with a value of P_a (see the figure), whereby $\tau = R \cdot C$ (τ is the so-called time constant of the RC circuit). Thus, the RC circuit is an electric analogy of the "calculated tissue" in that the saturation (and desaturation) processes of the tissue with the gas and the charge on the capacitor are mathematically identical.



Circuit equivalent to the "calculated tissue"

The electric analogy indicated permits construction of an electronic model of the tissues of a diver. For this it is sufficient to feed periodic trapezoidal voltage pulses simulating descent (or ascent) of a diver to a certain depth and a stay at this depth, and observe the voltage in the capacitors on the oscillograph.

We made up a "technical plan" for working out and producing a trapezoidal-pulse oscillator, a set of circuits and systems for restoring the base-line level to the C capacitor. In accordance with this plan I. A. Yudin worked out and produced an instrument which makes it possible to observe processes on the oscillograph screen which are mathematically identical with saturation and desaturation processes of the tissues of the diver with indifferent gases. In principle, this instrument may be used in calculations of decompression conditions, not to mention its possible use in teaching for illustrating of tissue saturation and desaturation.

Electrical analogies may be found for all magnitudes and processes of interest in connection with calculation of decompression conditions.

For example, the following are analogous:

C — the capacitance of the capacitor and the gas capacity of the tissue;

R — the electrical resistance and resistance of the blood system to the flow of the dissolved gas;

P — the electrical voltage of the capacitor and the gas tension in the tissue;

P_a — the emf of the source and the partial pressure of the indifferent gas in the lungs;

q — the electric charge on the capacitor and the quantity of gas dissolved in the tissues;

$i - \frac{dg}{dt}$ — the strength of the electric current in the circuit and the force of the gas flow to a given tissue in the blood system;

Fick's law (1855) for the diffusion rate corresponds to Ohm's law ($u = i \cdot R$);

a similar law for gas in the tissues and in the blood system corresponds to the law of conservation of electric charge.

When in the future, science obtains data about saturation processes of specific body tissues with gas, electrical analogies, when correctly selected, will make possible not only the use of well developed methods of the theory of electric circuits for calculating the decompression conditions, but also the construction of an electronic model of the body more perfected than the model mentioned above, and corresponding to Haldane's schema. The electronic model can greatly facilitate the calculation of specific conditions.

In addition to the electronic model, saturation of the "calculated tissue" with indifferent gas may be simulated by the simple hydraulic model of S. I. Sklyarenko and I. A. Kalinin (1953), which they proposed for the investigation of successive chemical reactions. It consists of two containers of a viscid fluid connected to a capillary tube in the bottom portions. One container simulates the lungs, the other (of cylindrical shape), the tissue; the fluid simulates an indifferent gas.

As will be seen below, with adherence to certain conditions this proves to be a mathematically exact and not just a qualitative analogy. Let us call the fluid level in the "lungs" container h_1; that in the "tissue" container h_τ (both levels are determined from the common arbitrary base line). The level h_x is the arbitrary time function which we are using; then level h_τ approaches h_x at a rate depending on the difference between the levels h_1 and h_τ, the width of the "tissue" container, and the resistance of the capillary to the movement of fluid. If the flow of fluid in the capillary is at the threshold, then Poiseuille's formula is justified (quoted from Frish and Timoreva, 1949). The latter may easily be transformed to a differential equation of the following type:

$$\frac{dh_\tau}{dt} = \frac{1}{\tau}(h_1 - h_\tau), \tag{3}$$

Here t is the time; $1/\tau$ is a constant for the given conditions, whereby $\frac{1}{\tau} = \frac{\pi}{8} \cdot \frac{R \rho g}{\eta l S_\tau}$ (4), where R is the radius of the capillary, l its length, S_τ is the cross-sectional area of the "tissue" container; ρ is the density of the fluid; η, its viscosity; g the acceleration of the force of gravity.

As pointed out above, equation (3) describes the processes in "calculated tissue" if we use Haldane's schema of the organism. In this case the fluid level h_τ is analogous to the gas tension in the tissue; while the level h_1 is analogous to the partial pressure of this gas in the lungs.

The hydraulic model of the tissue has an advantage over the electrical model because of its simplicity; however, it must be inferior to it with respect to speed and convenience of operation.

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P. M. Gramenitskii and P. A. Sorokin

THE MECHANISM OF RESPIRATORY AND CIRCULATORY CHANGES IN DOGS UNDER THE INFLUENCE OF HIGH OXYGEN PRESSURES

(K mekhanizmu izmenenii dykhaniya i krovoobrashcheniya u sobak pri deistvii vysokikh davlenii kisloroda)

Since the time of P. Ber (1878) the external picture of acute oxygen poisoning has been well known. Attention has been given to the successive development of signs of a toxic effect of high oxygen pressure. S. I. Prikladovitskii (1936, 1940) distinguishes three periods in the course of the convulsive forms of acute oxygen poisoning in animals: the first (preconvulsive) period is characterized by normal behavior with motor restlessness occurring only toward the end of this period with local signs of convulsion; the second (convulsive) period is expressed in clonic and tonic convulsions; the third (terminal) occurs without convulsions, and is characterized by progressive depression of respiration, ending in death.

A great number of papers have been written analyzing the mechanism of development of oxygen convulsions, chiefly from the aspect of a determination of the role of varicus nervous system centers in their origin (Dionesov, Kravchinskii, and Prikladovitskii, 1934; Ivanov, Kravchinskii, Prikladovitskii and Sonin, 1934; Prikladovitskii, 1936, 1940; Bean and Rottschaffer, 1938; Zhironkin, 1940; Voino-Yasenetskii, 1950, and others).

At the same time, there has been very little study and almost no analysis of changes in the main vital functions — respiration, and circulation — during acute oxygen poisoning. Papers existing on this subject are scattered. Behnke, Forbes, and Motley (1936) present data to the effect that in dogs anesthetized with sodium barbital the fall in blood pressure is an early constant and sign of oxygen poisoning and always precedes the convulsion. Bean and Rottschaffer (1937, 1938) note that in decerebrate dogs the earliest and most reliable sign of oxygen poisoning, indicating imminent convulsions, is hyperpnea accompanied by hyperventilation. There is considerable connection between the hyperventilation effect, which accelerates the development of oxygen poisoning, and aortic and carotid sinus nerves. According to their data, in decerebrate dogs under the influence of high oxygen pressure (5—6 atm) bradycardia develops, which decreases with denervation of the carotid sinuses and is eliminated by cutting the vagus nerves. Subsequently, during the course of the oxygen-induced convulsions, bradycardia is replaced by tachycardia, which, in their opinion, is connected with the selective block of efferent vagal fibers. They also observed in the experimental animals a moderate and considerable rise in the arterial blood pressure, which is at variance with data obtained

by Behnke and co-authors, 1936. By and large, information about the nature and mechanization of changes in respiration and circulation during oxygen poisoning is limited to this incomplete and controversial data.

Regular investigations have been made of respiration and cardiovascular activity in human beings (Zhironkin, 1956; Sorokin, 1958), showing that under an oxygen pressure of 2—2.5 atm there is a regular slowing of the heart rate, constriction of peripheral blood vessels, slowing of the circulation and reduction (at the beginning of the effect) of pulmonary ventilation. However, this data, understandably, applies only to the initial, preconvulsive period of the toxic effect of oxygen and, therefore, the dynamics and mechanism of development of respiratory and circulatory changes during oxygen poisoning and continues, on the whole, to be inadequately studied. This constituted the basis for making the corresponding experimental studies.

Method

The experiments were performed with urethane anesthesia on dogs of both sexes, weighing 12 to 17 kg. One hour before operation a solution of urethane was injected intramuscularly into the dogs (approximately two-thirds of the total dose) and intravenously after fixation to the table and brief stupefaction with ether (the remaining one-third of the dose). The total dose of urethane amounted, on the average, to 1.2 g per kg body weight. In the event of stimulation of respiration in dogs, 0.5—1.0 ml of a 2% morphine solution was injected aside from the urethane. To prevent blood coagulation in the blood-pressure recording system, an intravenous injection of Richter's heparin was given in a dose of 0.06 mg per kg.

After anesthetization a tracheotomy was performed. A cannula was injected into the left femoral artery for blood-pressure recording, and, depending on the purpose of the experiment, an approach to the vagus nerves, ansa subclavia, splanchnic nerves, or suprarenal glands was made.

The prepared animals were placed in a compression chamber. Their respiratory tracts were connected to a valve box; connected to its inspiratory valve was a rubber bag, to which oxygen was supplied from a tank located outside the chamber, through a connecting piece and a thick-walled rubber tube. The expiratory valve was connected to a water and gas meter; the latter had a rubber bag communicating with the air surrounding the chamber through a connecting pipe and valve. Thus, an isolated system was created whereby oxygen was supplied to the animal without entering the air filling the chamber.

In the chamber there was a kymograph for recording respiration, pulmonary ventilation and blood pressure. The record of respiratory movements was made by mechanical transmission of the respiratory excursions test to an Engelmann lever; the blood-pressure recording was made with an ordinary mercury manometer. The electromagnetic marker connected with the gas meter, equipped with electric contacts, recorded the pulmonary ventilation with an accuracy within 50 ml. In all the experiments a record of the electrocardiogram in three standard leads was made from time to time.

The pressure in the chamber in all experiments, with the exception of three controls, was increased to 6 atm. The medical oxygen supplied for the dogs' respiration contained no more than 1—2% nitrogen. The exposure to increased pressure varied in accordance with the aim of the experiment.

In all, 26 experiments were performed. In seven, the animals were exposed to the effect of high oxygen pressures without operation on the nervous system; in 11, vagotomy was performed, the ansa subclavia was cut, or the heart was completely denervated prior to the effect of oxygen or during different periods of oxygen poisoning; in eight the splanchnic nerves were cut and the suprarenal glands were isolated by the application of circular ligatures which separated them from the general circulation. In all experiments continuous observation was made of the development of signs of oxygen poisoning in the animals.

Results of the Investigations

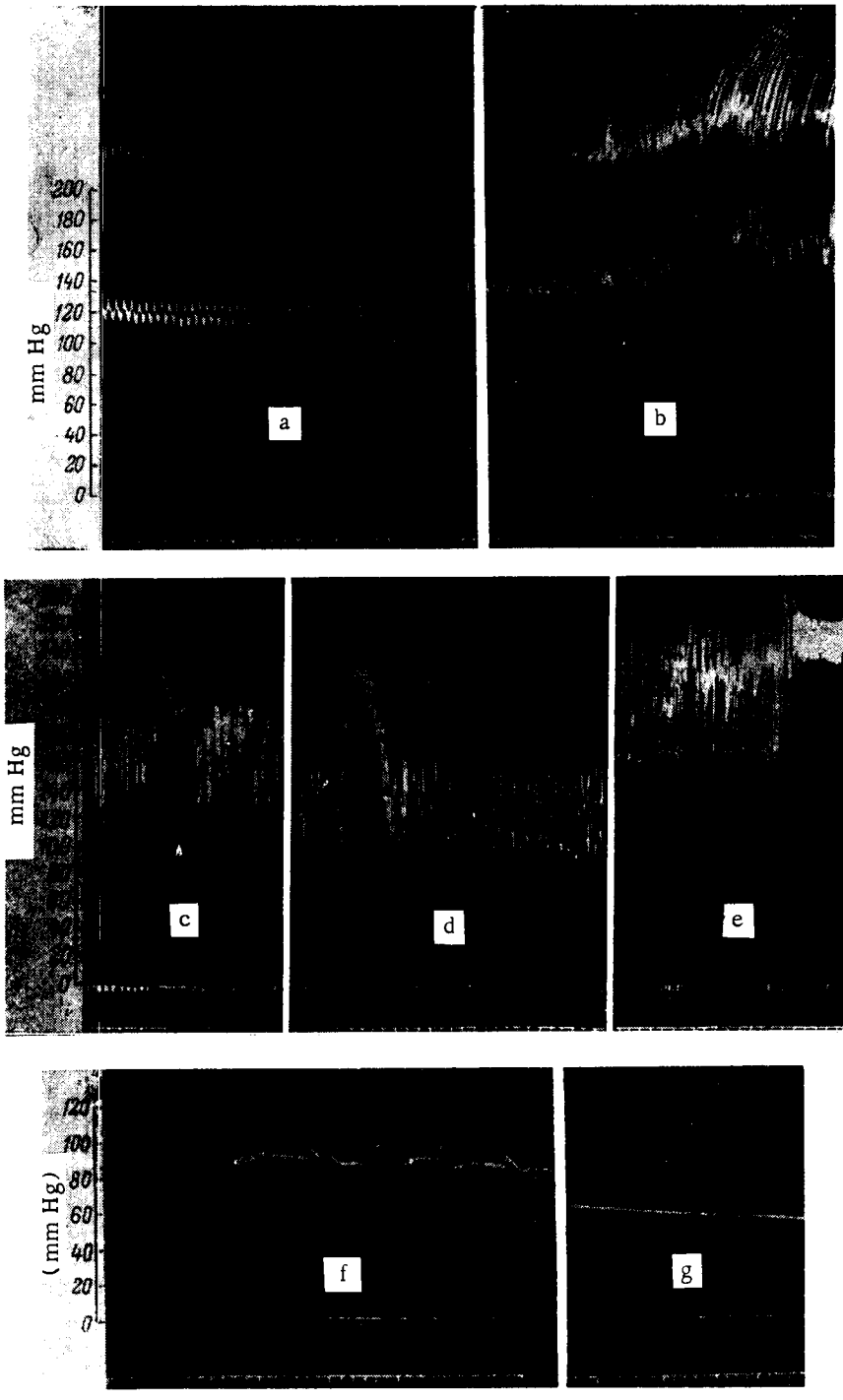
In animals with an intact nervous system under the influence of high oxygen pressures, regular and substantial changes in respiration and circulation occur. From the beginning of the effect of increased oxygen pressure to death of the animal, four periods may be distinguished in these changes. They are illustrated by kymograms presented in Figure 1.

Change in pulse, blood pressure, respiration, and pulmonary ventilation in the initial period of oxygen effect

No. of dog	Oxygen pressure (in atm)	Pulse		Blood pressure mm Hg		Respiratory rate		Pulmonary ventilation (in l/min)	
		initial	at beginning of oxygen effect	initial	at beginning of oxygen effect	initial	at beginning of oxygen effect	initial	at beginning of oxygen effect
4	5.0	97	52	100	90	18	12	2.1	1.7
5	6.0	120	96	119	110	23	15	3.6	4.0
6	the same	140	116	116	112	134	44	10.1	5.4
7	"	132	93	128	120	22	18	4.8	4.0
10	"	170	84	76	58	36	16	2.4	1.5
11	"	130	98	118	114	29	15	8.4	4.2
13	10.0	150	147	137	140	18	20	3.6	3.8
14	6.0	198	120	124	137	26	18	7.6	6.6
15	the same	168	94	96	123	36	32	7.4	5.6
16	"	180	132	100	102	18	16	4.5	4.2
18	"	174	146	96	90	54	34	6.0	3.0
19	"	186	156	86	86	36	23	4.2	3.4
21	"	170	124	115	127	22	16	5.4	4.6
23	"	165	150	128	125	78	18	11.5	4.0
24	"	194	116	87	76	22	20	3.4	3.3

FIGURE 1. Changes in respiration and blood pressure in dogs with an intact nervous system at various periods of oxygen poisoning under a pressure of 6 atm (experiment of 2 February 1957; dog No. 21, male, weight 20 kgs)

From top down: respiration, blood pressure, pulmonary ventilation (50 ml markings); time marking, one-second intervals. The kymograms have been recorded: a-during the period of compression while breathing oxygen (end of compression, 12 sec after beginning of the record); b-17 min after; c-25 min; d-45 min; e-55 min; f-67 min; g-74 min after beginning of the procedure.


mm Hg
200
180
160
140
120
100
80
60
40
20
0
a
b
mm Hg
c
d
e
(mm Hg)
120
100
80
60
40
20
0
f
g

The first, initial period (Figure 1, a) is characterized by slowing of the heart rate, and a reduction in the respiratory rate and pulmonary ventilation. No regular changes were found in the blood pressure; it increased very slightly, decreased somewhat, or remained practically unchanged.

The numerical data characterizing the functional changes listed are shown in the table. Reduction of the number of cardiac contractions occurred immediately after breathing oxygen under pressure, and in the majority of cases was very pronounced. The higher the initial frequency of the respiratory movements, the slower it became.

The initial period, expressed in the changes noted in respiration and cardiovascular activity under an oxygen pressure of 6 atm, was 8—12 min; under an oxygen pressure of 10 atm this period was practically absent.

The second period (Figure 1, b) was characterized by stimulation of respiration, increase in pulmonary ventilation and blood pressure, and some very slight increase in the heart rate. The pulse either returned to the initial level which obtained before the oxygen effect, or even failed to reach it. The blood pressure of animals with an intact nervous system exceeded the initial level by 10—50 ml in 14 experiments; in two, it increased to the initial figure. Respiratory rate underwent the most marked changes, its initial gradual deepening and increase progressing steadily and ending in marked dyspnea with pronounced hyperventilation. The respiratory rate increased by 14—15 respiratory movements a min; the pulmonary ventilation, by 4.8—9.6 l/min. The most pronounced degree of dyspnea occurred in the 16th—20th minute of action of compressed oxygen and constituted a true precursor of initial convulsive phenomena — marked and rapid twitching of the limbs, head, and later, of the trunk and abdominal muscles. In most dogs these twitchings appeared in the 20th—23rd minutes of the effect. They were usually connected with respiration and occurred in the expiratory phase. As the convulsive signs increased a further increase in blood pressure was noted, and at the same time a secondary progressive slowing of the pulse began. All this signified a transition to the third period of oxygen poisoning.

The third period (Figure 1, c, d)* was characterized by development of typical convulsive attacks involving the entire body, with clearly expressed tonic and clonic components. Thereby, the blood pressure remained high; during each convulsive attack it increased considerably (30—40 mm Hg). Between the convulsive attacks the pulse was slow; during them its frequency increased considerably. Subsequently, a lessening or even a temporary cessation of convulsive attacks occurred, which usually coincided with maximum slowing of the heart rate, and a typical vagus pulse recorded on the kymograph (Figure 1, d). On the electrocardiogram taken during this period, sinus bradycardia was noted with marked respiratory variations of the R-R intervals. Of nine dogs in which an electrocardiogram tracing was made during this period, the slowing of the heart rate in six ended in the development of nodal (A-V) rhythm and in two in an A-V block; in one case it was partial and in the other, complete.**

* In view of the fact that convulsive attacks caused a driving of the respiratory record, the latter is not shown. The changes in respiration may be judged by the record of pulmonary ventilation.

** Detailed electrographic data are presented in the article by P.A.Sorokin, "Changes in the Electrical Activity of the Hearts of Animals under the Influence of High Oxygen Pressures", included in the present collection.

The number of cardiac contractions came to 24 per min. With the occurrence of nodal rhythm or heart block the blood pressure always fell; however, in the majority of cases it did not drop below the level recorded before the influence of high oxygen pressure. Subsequently, a depression of respiration occurred with periods of apnea (Figure 1, e; record of pulmonary ventilation). Simultaneously, the blood pressure again increased somewhat with an intact vagal pulse. The duration of the third period was usually 12—20 min.

The transition to the fourth and final period occurred suddenly; it was expressed in the fact that all at once, without any procedures by the experimenter, the slow heart rate was replaced by a marked sinus tachycardia, accompanied by a rapid rise in the blood pressure to figures of the order of 250—280 mm Hg (Figure 1, e). The blood pressure, which remained high for a certain time, began to drop steadily; this drop continued with tachycardia increasing at the same time, until the animal's death. With the appearance of tachycardia convulsive attacks were renewed; now they were mainly of a tonic nature (extension of the entire body with marked extension of the limbs, and opisthotonus). Each convulsive attack during this period, as in the preceding one, was accompanied by a marked brief rise in blood pressure (Figure 1, f).

Subsequently, respiration became agonal and stopped; simultaneously, the convulsions stopped. Respiratory arrest occurred about 1 hr after the beginning of the effect of high oxygen pressure; cardiac activity continued for another 10—20 min; the blood pressure dropped uniformly and steadily (Figure 1, g). After respiratory arrest, when the blood pressure had dropped to the base line and no pulse waves were recorded on the kymogram, precordial and ventricular waves were recorded on the electrocardiogram for a certain period. Rapid sinus rhythm was again replaced by slowing and gradual disruption of atrioventricular conduction. The ventricular complexes on the electrocardiogram became progressively slower and shortly afterwards disappeared entirely; only precordial waves remained for a brief time, and then gradually disappeared.

The procedures performed on the parasympathetic and sympathetic nerves and suprarenal glands substantially altered the cardiovascular and respiratory reactions to the effect of high oxygen pressures. The cardiograms shown in Figure 2 reflect the typical changes in circulation and respiration during the development of oxygen poisoning in the animals after preliminary sections of both the vagus nerves in the neck. In these cases the reactions characteristic of the first period of oxygen poisoning disappeared: neither a reduction of pulmonary ventilation nor a slowing of the pulse was noted. In vagotomized dogs there was a complete absence of typical changes in cardiac activity in the form of bradycardia, and A-V conduction disorders in the third, convulsive period of oxygen poisoning (Figure 2, d). Developing initially after vagotomy, tachycardia remained during the convulsive attacks and in the intervals between them. The transition to the fourth period was expressed in a sudden blood pressure rise to extremely high figures (Figure 2, e), a great increase in the heart rate, and in long-lasting apnea. The final stage of oxygen poisoning in vagotomized dogs (Figure 2, f, g) was approximately the same as in intact dogs, i.e., before final cardiac arrest decreased conduction occurred leading to complete A-V block and ending in an initial disorder of the ventricular function. In the second period of oxygen poisoning dyspnea in

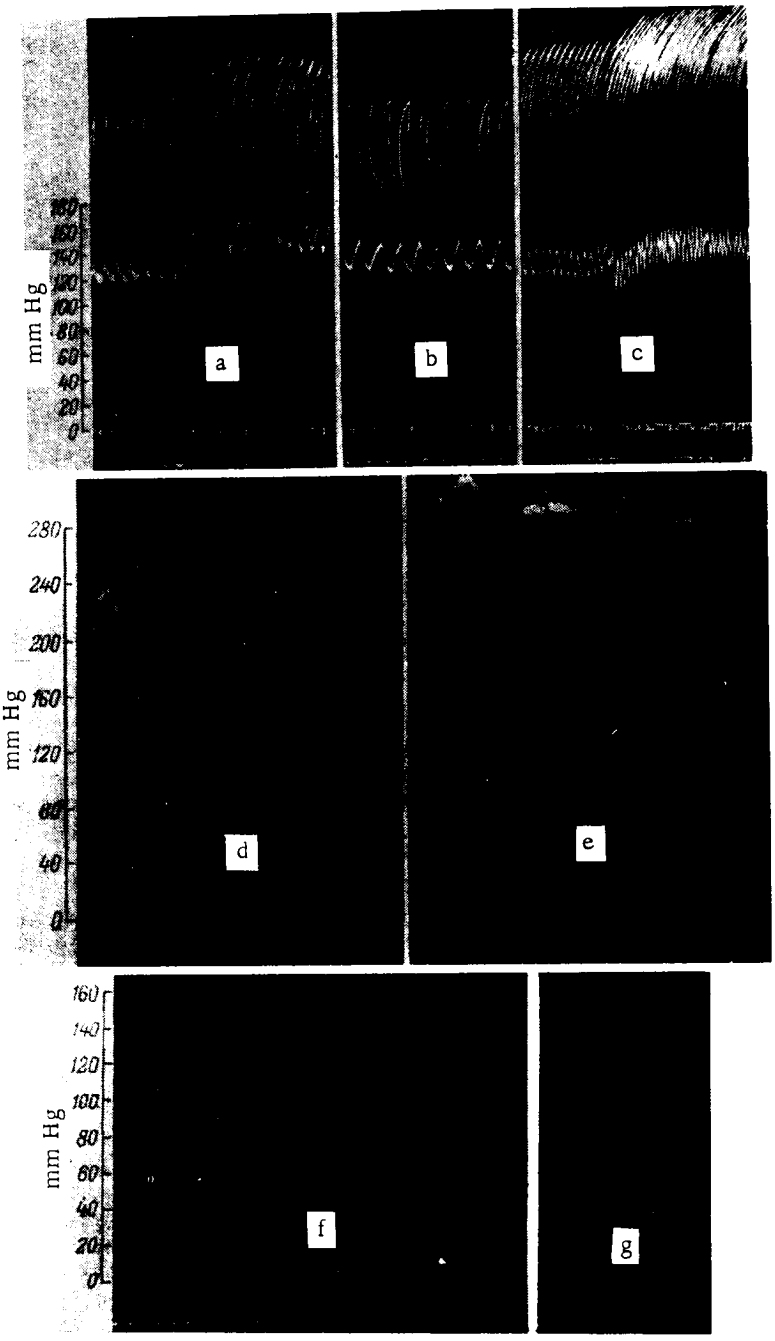


FIGURE 2. Changes in respiration and blood pressure of a vagotomized dog at various periods of oxygen poisoning under a pressure of 6 atm (experiment of 4 February 1957; dog No. 22, male, weight 16.3 kg)

The kymograms were recorded: a-during bilateral vagotomy (the time of vagotomy is noted on the bottom curve); b-9 min after vagotomy under ordinary conditions; then, while breathing oxygen; c-17 min after beginning of the procedure; d-[illegible] min after; e-39 min; f-58 min; g-69 min after beginning of the procedure. Rest of key same as for Fig. 1.

the vagotomized dogs was very marked. The precursor of convulsions and general convulsive paroxysms occurred somewhat earlier than in intact animals (after 12—17 min instead of 16—25 min) and were distinguished by their greater degree. Thus, the total lifespans of the vagotomized animals under conditions of high oxygen pressure were shorter; death occurred 10—20 min earlier than in intact animals.

To ascertain whether this was the result of the vagotomy itself, we performed a control experiment in which the dog was not exposed to the oxygen effect for more than 2 hrs after cutting of the vagus nerves. During this entire period the pulse, respiratory rate, blood pressure, and pulmonary ventilation which had become established on a new level after the vagotomy, remained without any essential changes.

Experiments with operation on the sympathicoadrenal system showed that it played an exceptional part in the development of oxygen poisoning. After the ansa subclavia and splanchnic nerves had been cut and the suprarenal glands completely isolated, the blood pressure under ordinary conditions became established at low levels; the respiration became exceptionally smooth and rhythmical, with a somewhat reduced pulmonary ventilation (Figure 3, a, b, c).

Increased oxygen pressure of 6 atm for over 2 hrs did not greatly affect respiration and blood circulation (Figure 3, d, e, f, g). Periodic moderate dyspnea was noted, with increased pulmonary ventilation, but not more than 2—2.5 times that of the intitial time. At the same time, arterial pressure increased by 25—35 mm of mercury and then returned to its initial level. Slight decrease of the pulse (10—15 beats per min) was noted either at the beginning of the experiment or during its performance; the vagus pulse was entirely absent. Spasms were completely absent or noticeable only slightly on bending of the body, during 2 or even 3 hrs of exposure to pressure, though appearing periodically toward the end of the experiment. There was no sign of phenomena threatening the life of the animals throughout the experiments. The animals were transferred to air respiration and compression was carried out. By stimulating at the same time the vagus nerve by induction current, we assured the presence of characteristic vagal reaction on the heart (Figure 3, h).

Therefore, the absence of typical vagus effects on the heart during the course of oxygen poisoning was not caused by disruption of the parasympathetic innervation of the heart muscle, but by procedures performed on the sympathetic nerves and suprarenal glands.

Complete isolation of the suprarenal glands with cardiac innervation and splanchnic nerves intact also caused a marked change in the course of oxygen poisoning (Figure 4). In these cases the animals also tolerated a two- or even three-hour effect of oxygen under a pressure of 6 atm without showing any critical respiratory or circulatory disorders. A change in these functions during the course of this effect, as shown by kymograms in Figure 4, could not be compared with the reactions of intact animals or were similar to what occurred in dogs with isolated suprarenal glands, a desympathized heart and cut splanchnic nerves. It is significant that simple isolation of the suprarenal glands also led to a considerable reduction of vagal effects on the heart; in these cases, both at the beginning of the procedure and subsequently, a comparatively slight slowing of the heart rate occurred, true bradycardia with deep-seated conduction disorders was never noted.

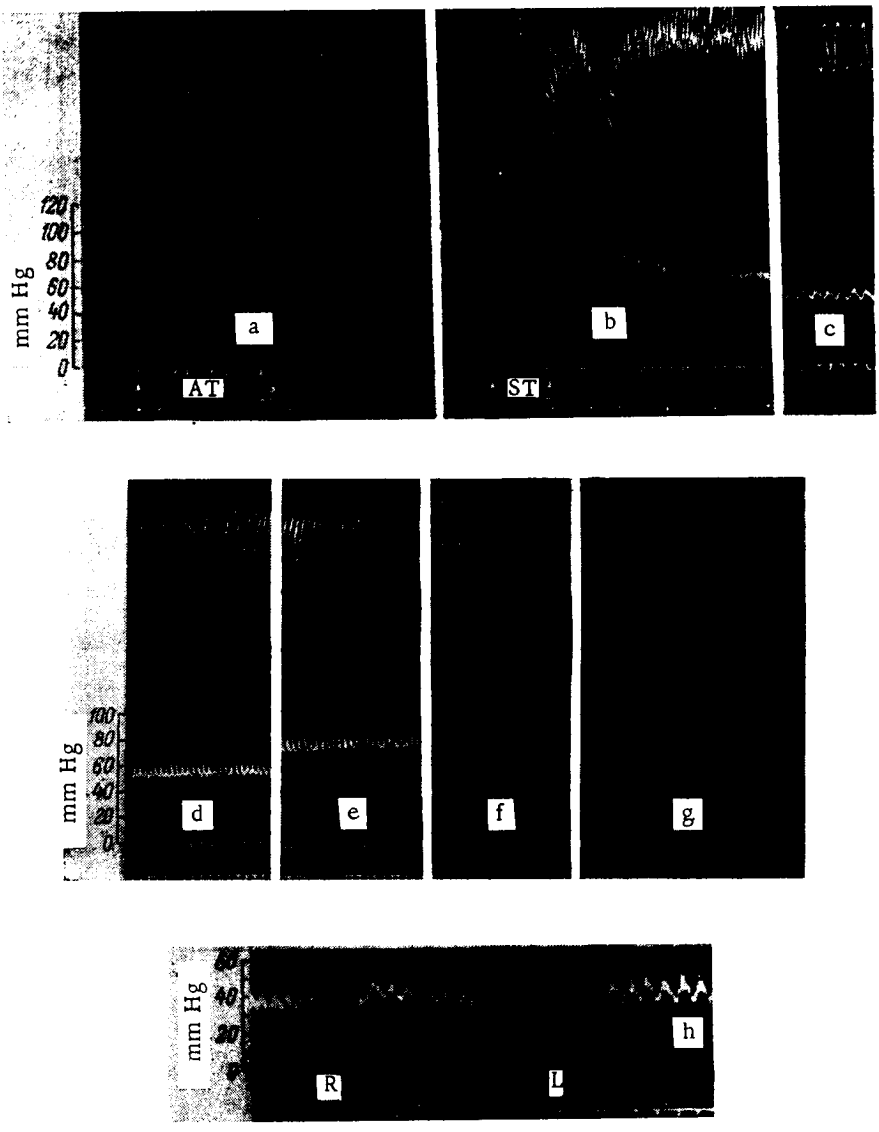


FIGURE 3. Changes in respiration and blood pressure of dogs with ansa subclavia and splanchnic nerves cut and suprarenal glands isolated, under the influence of increased oxygen pressure of 6 atm (experiment of 1 February 1957); dog No. 20, male, weight 16.5 kg)

Kymograms a, b, and c were recorded before compression: a — with cutting of the ansa, AT; b — with cutting of the splanchnic nerve, ST; c — 4 min after isolation of the suprarenal gland; d, e, f, and g — during the breathing of oxygen under pressure for 3 min; h — 19 min after beginning of the procedure; f — 65 min; g — 137 min after. The kymogram h was recorded 10 min after decompression. The arrows indicate stimulation of the right and left intact vagus nerves with an induced current.

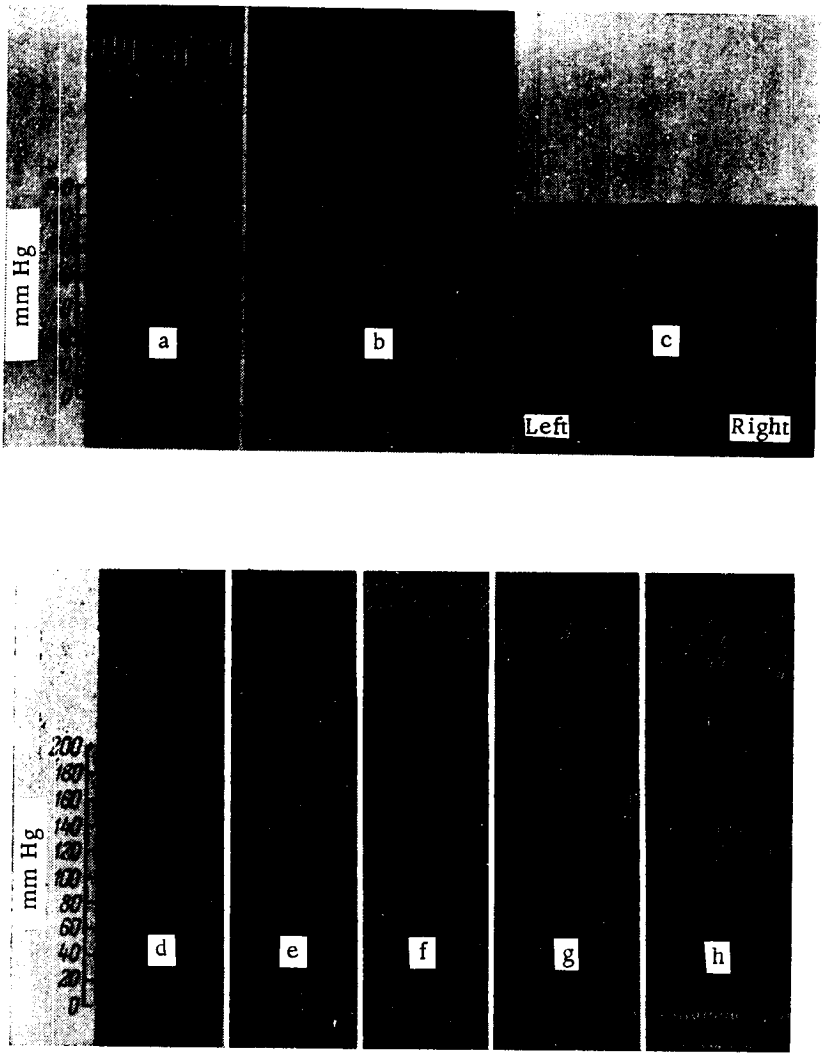


FIGURE 4. Changes in respiration and circulation in a dog with isolated suprarenal glands and intact splanchnic and cardiac nerves under the influence of increased oxygen pressure of 6 atm (experiment of 14 February 1957; dog No. 25, female, weight 10 kg)

Kymograms a, b, and c were recorded before compression: a — before the procedure; b — 5 min after isolation of the suprarenal gland; c — 8 min after (a check on the integrity of the splanchnic nerves). The arrows indicate stimulation of the left and right nerves by an induced current. Kymograms d, e, f, and h were recorded during the breathing of oxygen under pressure; d — 12 min after beginning of the procedure; e — 38 min after; f — 88 min; g — 106 min; h — 126 min after beginning of the procedure. The rest of the key is the same as for Figure 1.

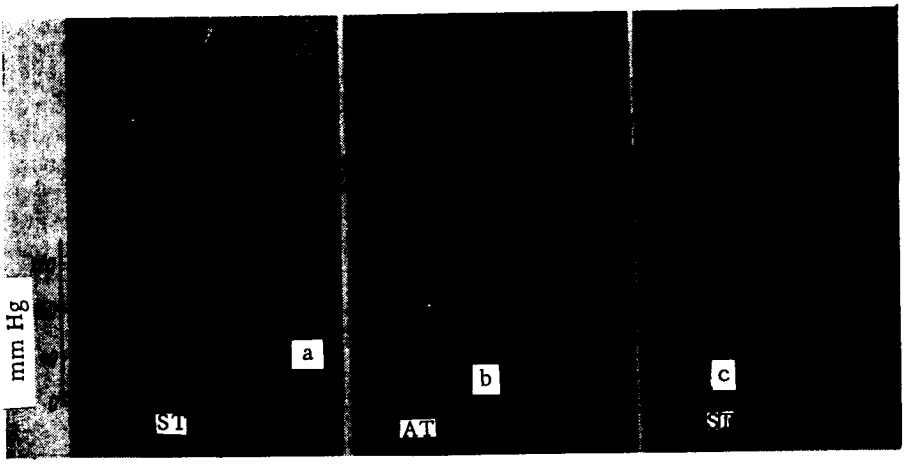


FIGURE 5. Changes in respiration and blood pressure in a dog during vagotomy, cutting of the ansa subclavia and splanchnic nerves in the second period of oxygen poisoning (experiment of 31 January 1957; dog No. 19, female, weight 12,5 kg).

The kymograms were recorded: a — 20 min after beginning of breathing of oxygen under a pressure of 6 atm; b — 26 min after; c — 31 min after. VT, vagotomy; AT, cutting of the ansa; ST, cutting of the splanchnic nerves. The rest of the key is the same as for Figure 1.

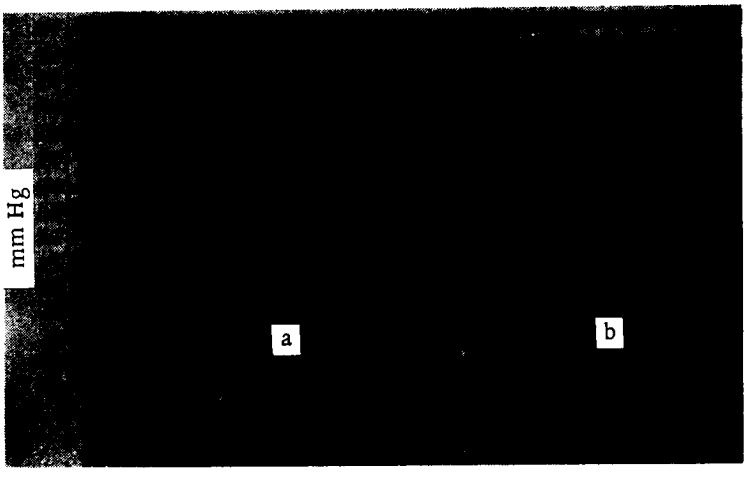


FIGURE 6. Changes in respiration and blood pressure in a dog vagotomized in the third period of oxygen poisoning (experiment of 17 January 1957; dog No. 4, male, weight 19,6 kg)

The kymograms were recorded as follows: a — 59 min after the beginning of breathing oxygen under pressure of 6 atm; b — 64 min after. The arrow indicates the moment of bilateral vagotomy. The rest of the key is the same as for Figure 1.

Typical oxygen convulsions did not develop in dogs with isolated suprarenal glands; reactions were limited to convulsive twitchings of the majority of muscles, which occurred usually in the second hour (Figure 4, g) and were subsequently replaced by weak and slow tonic episodes of body extension.

Procedures performed on various nerves made it possible to determine their part in the development of circulatory reactions at various stages of oxygen poisoning. Bilateral vagotomy in the second period of oxygen poisoning, characterized by increase in dyspnea and blood pressure, failed to show any appreciable effect (Figure 5, a). Cutting of a cardiac branch of the sympathetic nerve during this period, conversely, had pronounced aftereffects. In this case (Figure 5, b) there was an appreciable reduction of blood pressure and simultaneously cardiac contractions decreased by 40—45 beats a min. Cutting of splanchnic nerves, performed in the same period after cutting of the ansa (Figure 5, c), caused an additional blood pressure reduction, but did not affect the pulse rate. In the third, convulsive period, when marked bradycardia developed in the interval between convulsive paroxysms, and at the end of this period when bradycardia reached its greatest degree, the cutting of the vagus nerves always produced striking effects (Figure 6, a, b). A pronounced vagal pulse with A-V conduction disorders was replaced by very marked sinus tachycardia; blood pressure suddenly rose 60—80 mm Hg, increased even further and, after remaining for a certain time at maximum figures, began to drop gradually. Generally, under these conditions, the changes in cardiovascular activity during vagotomy very much resembled those which in the intact animal signified a sudden transition to the fourth and final period of oxygen poisoning. Cutting the vagus nerves in the early periods of the procedure led to a more rapid development of and increase in convulsions; a disruption of the sympathetic innervation of the heart and particularly cutting of the splanchnic nerves caused convulsive phenomena to be delayed and lessened.

Discussion of Results

The results of the investigation showed that during the first period of an oxygen pressure of 6 atm, there is a regular slowing of heart contractions and respiration, and a reduction of pulmonary ventilation. Similar changes with lower figures for the partial oxygen pressure (1 and 2 atm) were noted in animals by a number of authors (Anthony, 1940; Keys, Stapp and Violante, 1943; Whitehorn, Edelmann, and Hitchcock, 1946) as well as in human beings (Sorokin, 1958). There is direct data concerning the reflex nature of these functional changes, and particularly the role of sinus and aortic nerves in their occurrence (Bean and Rottschaffer, 1938; Dumke, Comroe, 1942). The results of our experiments with preliminary vagotomy of animals show the decisive role of vagus nerves in the development of the functional changes mentioned, and lead to the supposition that not only efferent parasympathetic fibers (through which the inhibitory influences of the heart are realized) but also afferent nerve conductors from the pulmonary and aortic receptors are of importance here.

The initial respiratory and circulatory changes noted under the influence of a high partial oxygen pressure must evidently be evaluated, in accordance with the majority of authors, as adaptive compensatory reactions of the body which slow the rate of tissue saturation with oxygen and, therefore, delay oxygen poisoning.

The second period is characterized by a marked, progressively increasing dyspnea, and an increase in heart rate and blood pressure. As experiments have shown, the sympathetic nervous system and suprarenal glands play a decisive part in the development of these reactions. The vagus nerves show no effect here. Their influence is found again in the third, convulsive period, when bradycardia develops between the paroxysms and continues to progress. The actual paroxysms are characterized by marked changes—of strikingly sympathetic nature—in cardiovascular activity. Therefore, during this period a distinctive alternation of sympathicoadrenal and parasympathetic reactions occur in the circulatory system, when, against the general background of progressively increasing vagal influences, they are temporarily disrupted, leaving aftereffects. Under these conditions, the vagus nerves and associated bradycardia play a beneficial role, contributing to an economy of the functional reserves of the heart, as occurred, for example, in cases of marked hypoxemia and asphyxia. In addition, the sensory pulmonary nerves included in the vagus nerves limit the irradiation of excitation from the respiratory center to the motor nerve center (Vinokurov, 1952) and thereby moderate the convulsions, which, as has been pointed out, are usually connected with respiration.

The beneficial role of the vagus nerves in the course of oxygen poisoning is confirmed directly by the fact that in vagotomized dogs the convulsions occurred more quickly, were distinguished by greater strength, and the lifespans were usually shorter under the influence of high oxygen pressure than in intact animals. It is significant that in the third period of oxygen poisoning such phenomena are noted as nodal rhythm or partial or even complete A-V block, which clinically are usually considered signs of organic cardiac pathology. Here, these cardiac rhythm disorders are of a purely functional nature and determined entirely by the effect of the vagus nerves of the heart.

The fourth and final period is characterized by a sudden and definitive breakdown of parasympathetic effects on cardiovascular activity, replacement of them by pronounced sympathetic effects, which probably indicate a fatal outcome in oxygen poisoning.

Slowing of the pulse and cardiac conduction disorders in the agonal stage of oxygen poisoning are evidently explained by a deep-seated toxic effect of oxygen on the cardiac tissues, rather than by nervous influences.

Experiments with isolation of the suprarenal glands and cutting of the ansa subclavia and splanchnic nerve show the exceptional part played by the sympathic and renal systems in the development of oxygen poisoning. With respect to the suprarenal glands the results of our experiments were in agreement with the data of Gershman, Gilbert, Nye, Price, and Fenn, (1955), who also observed a postponement of death in mice with suprarenal glands removed, under the influence of high oxygen pressure. The authors connect this effect chiefly with the hormones of the suprarenal cortex, which is, to a certain degree, in agreement with data of Bean (1952), who found that an essential part in the development of oxygen poisoning is played by the adrenocorticotropic hormones of the hypophysis.

Our data does not provide a basis for denying the part played by cortical hormones of the suprarenal glands in the development of oxygen poisoning; however, it undoubtedly indicates the exceptional significance of the sympathicoadrenal system under these conditions. It is especially noteworthy that in animals with the suprarenals isolated and the splanchnic nerves and sympathetic tracts to the heart cut, but with the vagus nerves intact, there were no parasympathetic influences on the heart characteristic of intact animals during the course of oxygen poisoning. Hence, it follows that in acute oxygen poisoning the parasympathetic effects on the heart are realized only with preservation of the function of the sympathicoadrenal system. Therefore, very unique relationships are created: on the one hand, the sympathicoadrenal system determines, to a considerable degree, all the basic manifestations of the toxic effect of high oxygen pressure and eliminates, so to speak, the protective cardiovascular reactions of a parasympathetic nature; on the other hand, it is necessary for the manifestation of these protective reactions.

Conclusions

1. During acute oxygen poisoning four periods should be distinguished in anesthetized animals (dogs):

a. The first, initial period, characterized by reduction of pulmonary ventilation and slowing of cardiac activity, is the period of adaptive reactions of the body. The vagus nerves play the main part in these protective reactions.

b. The second, preconvulsive period, expressed in hyperventilation, tachycardia, and an increase in the arterial blood pressure, reflects a marked stimulation of the sympathicoadrenal systems. These reactions are unfavorable and accelerate the development of oxygen poisoning.

c. The third, convulsive period is characterized by gradual slowing of the heart rate, which during the convulsive attacks is replaced by tachycardia with an additional pressor effect. At the end of this period, against the background of respiratory depression, there is a predominance of parasympathetic effects on the heart which lead to bradycardia, nodal rhythm or heart block. These serious disorders of cardiac rhythm are reversible and disappear after vagotomy.

d. The fourth, terminal period is characterized by a sudden replacement of parasympathetic by sympathetic reactions, which is expressed in a very marked and rapid rise in blood pressure and increase in the heart rate (sinus tachycardia). After respiratory arrest the blood pressure steadily drops, but cardiac activity is maintained. The bradycardia and heart block which occur toward the end of the period are not eliminated by vagotomy.

2. Preliminary section of the vagus nerves eliminates the slowing of the heart rate in the first and third periods of oxygen poisoning, accelerates the occurrence of convulsive paroxysms, and shortens the lives of the animals when compressed oxygen is used.

3. Preliminary isolation of the suprarenal glands prolongs considerably the lifespans of the animals and under an oxygen atmosphere, with pressure of 6 atm it delays and lessens the development of convulsive

phenomena. A similar but even more pronounced effect is exerted when this procedure is combined with cutting the splanchnic nerves, which results in elimination of excessive excitation of the sympathicoadrenal system, increase in the deposition of blood and reduction of the blood supply of the body tissue, as well as a reduction of oxidation processes.

4. After isolation of the suprarenal glands, and cutting of the splanchnic and cardiac sympathetic nerves in animals during oxygen poisoning, no cardiac parasympathetic reactions characteristic of the intact organism developed, despite the integrity of the vagus nerves.

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PATHOLOGICAL CHANGES IN THE LUNGS OF ANIMALS UNDER THE INFLUENCE OF HIGH OXYGEN PRESSURES

(O patomorfologicheskikh izmeneniyakh v legkikh u zhivotnykh pri deistvii vysokikh davlenii kisloroda)

It is well known that increased oxygen pressures exert a toxic effect on the body. The studies of a number of authors have shown that in animals which died after exposure to the oxygen effect under ordinary pressure, pulmonary involvement was primary, taking the form of atelectases of different sizes and degrees, hypostatic congestion, edema, hemorrhages and inflammatory changes (Smith, 1899; Achard, Binet, and Leblanc, 1927; Binet, Bochet, and Briskier, 1939; Kaunitz, 1942; and others). At the same time, hypostatic congestion has been found in other internal organs (heart, liver, spleen, kidneys, suprarenal glands, and intestines).

The pathological changes in the lungs are usually demonstrable only after the end of a certain period after the beginning of the oxygen effect. Karsner (1916) found hypostatic congestion of the lungs in rabbits 24 hrs after the beginning of their stay in an atmosphere of 80—90% oxygen, an inflammatory reaction in the bronchial tubes after 48 hrs, and signs of bronchopneumonia after 72 hrs.

Grognot and Chome (1955), in experiments with guinea pigs, observed a cloudy swelling of alveolar cells and a change in their structure between 3 and 6 hrs after the animals had first been placed in an atmosphere of oxygen. Beginning with this time, the phenomena extended to all lobes in the lungs. According to their data, this reaction is reversible and disappears after about 24 hrs.

Under the influence of higher oxygen pressure (over 3 atm) the animals showed similar pathological changes in the lungs (Bronstein and Stroink, 1912; Dionesov, Kravchinskii, and Prikladovitskii, 1934), but less pulmonary involvement was noted than after the influence of oxygen under ordinary pressure. These authors attribute this to the fact that under high oxygen pressures the animals die more quickly, and no pronounced changes can develop in the lung tissue.

Pichotka and Kühn (1947) emphasize that in guinea pigs and rabbits which die as the result of the oxygen effect under ordinary pressure, a pathological picture is observed characteristic of hypoxemia (focal necrosis in the heart muscle, changes in the periphery of the hepatic lobules with central vacuolation of them and fatty degeneration), whereas such changes are not found in animals exposed to the effect of high oxygen pressure (3.5—5.8 atm).

With respect to the origin of pulmonary involvement in oxygen poisoning, various opinions have been expressed. Most authors believe that pathological

changes in the lungs are caused by the irritating effect of oxygen on the respiratory tract and pulmonary alveoli (Smith, 1889; Bean, 1945; and others).

Ohlsson (1947), on the basis of his studies, concluded that pulmonary involvement under conditions of breathing oxygen does not occur on the "air" side, because of the irritating effect of oxygen, but on the "blood" side, as the result of injury to the capillary wall by increased concentrations of carbon dioxide, the transport of which, as is well known, is disturbed under conditions of hyperoxia.

I. A. Sapov (1953) ascribed importance to nerve reflex influences in the development of pulmonary lesions under a compressed oxygen effect. He showed that bilateral block or section of the vagus nerve increases pulmonary involvement, whereas cutting the posterior roots of C 6—7 to D 4—5, denervation of the carotid sinus and aortic regions or atropinization considerably lessens or prevents development of the pathological process in the lungs.

It is evident from the data presented that there are only scattered reports in the literature dealing with the study of pathological characteristics in acute oxygen poisoning, and to date there is no agreement as to the mechanism of pulmonary involvement under the influence of increased oxygen pressures. This fact was the basis for the present study.

Method

The first series of observations was made on 12 guinea pigs exposed to the effect of oxygen under a pressure of 5.5 atm. To exclude vagal effects, six animals were first injected subcutaneously with atropine in a dose of 1 mg per kg. Two guinea pigs were used as controls.

The experiments were performed in a steel chamber with a capacity of 65 l. In order to remove excess carbon dioxide, the chamber was ventilated every half hour for 4—5 min, and supplied with gauze bags filled with soda lime. In different experiments the carbon dioxide content of the chamber ranged from 0.05—0.2%; the oxygen content, from 92—96%; the nitrogen content, from 4—8%.

The second series of experiments was performed on dogs anesthetized with urethane. The oxygen supplied to the chamber for the animal contained 1—2% nitrogen. Of 15 dogs, one was exposed to the effect of oxygen at ordinary pressure; the others, at a pressure of 6 atm. Nine dogs died from the effect of compressed oxygen. The others were killed with gas embolism or an electric current.

The animals were dissected 20—60 min after death. A histological study was made of the lungs, heart, liver, spleen, kidneys, intestines, and in a number of cases, the brain. Preparations were stained with hematoxylin and eosin by the van Giesson method; in addition, the heart muscle was stained with Heidenhain's iron hematoxylin.

Results of the Investigation

In the first series of experiments, dissection of guinea pigs which died of acute oxygen poisoning revealed primarily the pulmonary involvement. External examination showed bluish-purple and somewhat collapsed areas of atelectases, usually multiple, and most often located along the lung margins, chiefly in its posterior portions. On section they were either superficial or penetrated more deeply into the lung tissue, not uncommonly including considerable sections of one lobe or another. The lungs were

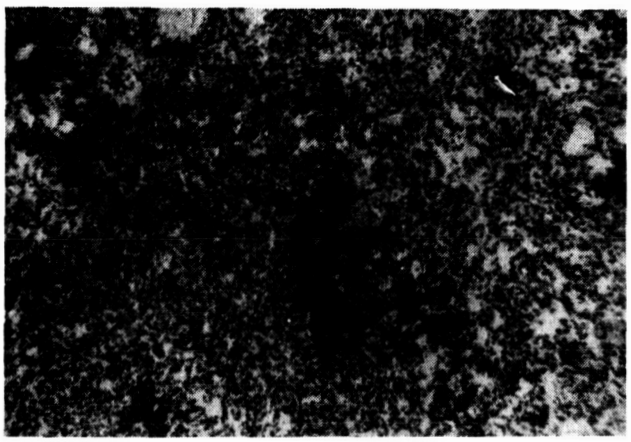


FIGURE 1. Guinea pig No. 29. Experiment of 24 December 1956. Atelectasis of lung tissues with edema and the appearance of red blood cells in the alveoli as well as areas of eosinophilic infiltration (dark accumulations). Magnification 80 ×

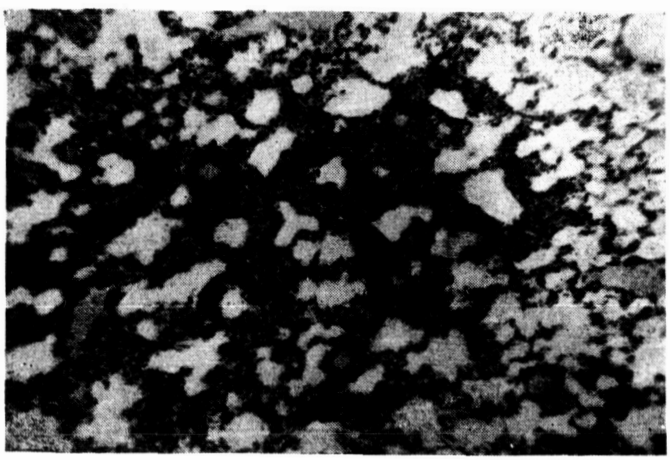


FIGURE 2. Guinea pig No. 34. Experiment of 19 December 1956. Thickening of the alveolar septa in connection with edema and overfilling of the capillaries with blood. Magnification 80 ×

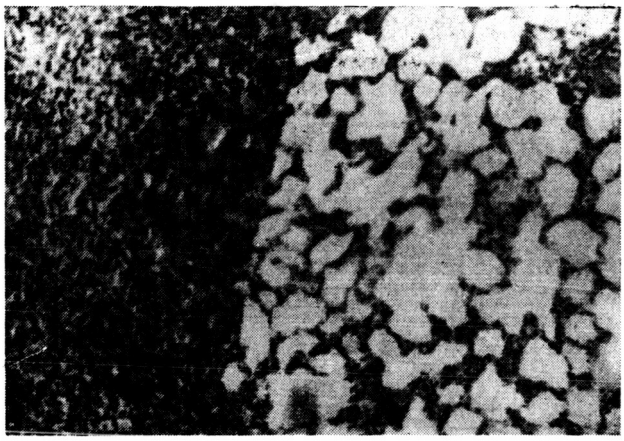


FIGURE 3. Guinea pig No. 23. Experiment of 17 December 1956. Boundary between the atelectatic area and the emphysematous portion of the lung. Magnification 80 ×

always congested. Pronounced edema in them was noted in only one case. The cardiac chambers of the right side and that of the left atrium were usually dilated and overfilled with blood, whereas the left ventricles were not uncommonly contracted. The coronary blood vessels of the heart were dilated and congested. Sometimes, occasional small subepicardial hemorrhages were found, usually in the area of the right coronary sinus. As a rule, the abdominal organs were congested, particularly the liver.

Histological changes in the lungs were characterized by marked venous and capillary dilatation and congestion, particularly in areas of atelectasis (Figure 1). In some places the small arteries were dilated, and in others they were constricted. Around the blood vessels (arteries and veins) edema

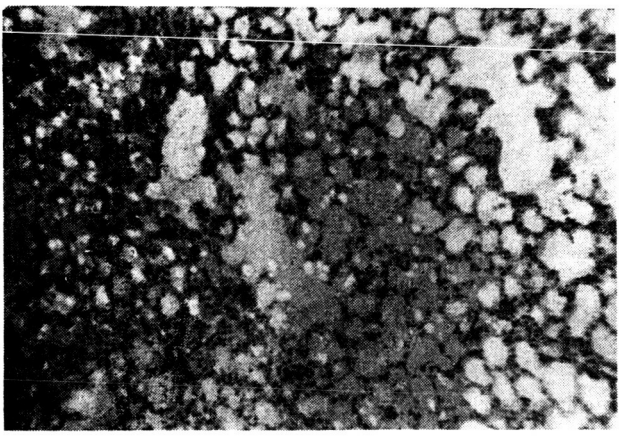


FIGURE 4. Guinea pig No. 32. Experiment of 3 January 1957. The animal was first atropinized (dose of 1 mg per kg). Pulmonary edema. Magnification 80 ×

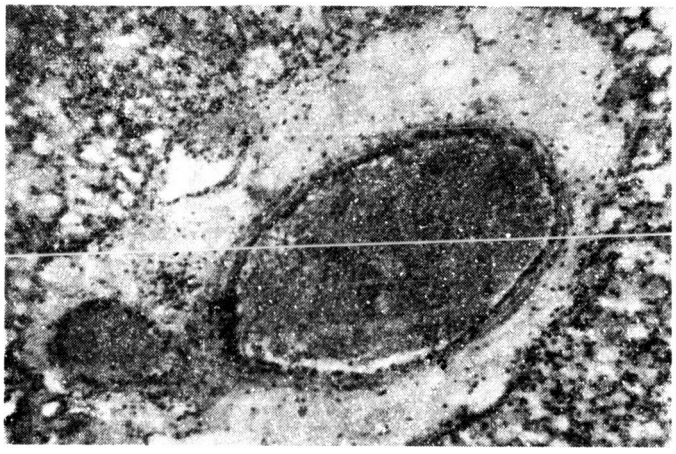


FIGURE 5. Guinea pig No. 32. Experiment of 3 January 1957. Edema around markedly dilated and congested pulmonary vein in the midst of an atelectatic area. Magnification 80 ×

was found. The walls of the alveoli were usually thickened because of edema and overfilling of the capillaries with blood (Figure 2). The lumina of the alveoli not uncommonly were filled with a serous fluid admixed with erythrocytes. In the interalveolar and peribronchial tissues accumulations of eosinophils frequently were found to a greater or lesser degree, Sections of more or less pronounced atelectasis alternated with areas of emphysematous alveoli (Figure 3). The areas of atelectasis were located both subpleurally and in the depths of the lung tissue. In various cases, there was a small quantity of mucus in the bronchial lumen.



FIGURE 6. Dog. No. 23. Experiment of 31 January 1957. Perivascular edema with hemorrhages in the brain tissue. Magnification 80 ×

In the heart muscle capillary dilatation was noted with occasional small hemorrhages in the intermuscular tissue. In the liver, kidneys and spleen the picture of pronounced hypostatic congestion was observed. In guinea pigs which had first been atropinized, areas of atelectasis were noted in the lungs, with congestion of pulmonary vessels, and edema in the alveoli (Figure 4) and perivascular connective tissue (Figure 5). In three animals no eosinophilic infiltration was found in the lungs.

In a number of experiments guinea pigs which had survived exposure to compressed oxygen, subsequently (after 24 hrs or several days) died of severe bronchopneumonia. In one of the guinea pigs the acute pneumonia developing after the action of compressed oxygen did not disappear but changed into the chronic form.

In the second series of experiments morphological changes were studied in 15 dogs. In the five control animals, no operations were performed either on the nervous system or on the suprarenal gland. Of this group, three dogs died of acute oxygen poisoning, the other two, exposed to the action of compressed oxygen for 35—36 min, remained alive and were killed after decompression.

For the purpose of characterizing pathological changes in the animals of this group, autopsy and histological data are presented on dog No. 23, which died in the 64th minute of inhalation of oxygen under a pressure of 6 atm.

On opening into the lungs, many cyanotic areas of atelectasis were noted chiefly in the posterior portions, not only in the marginal portions of the lobes but also in areas near the roots. In the tissue of the anterior mediastinum, multiple small hemorrhages were seen; in the epicardium, scattered punctate hemorrhages. The atria and right ventricle of the heart were markedly dilated and overfilled with blood. In the liver, kidneys, spleen, mesenteric blood vessels and pia mater, hypostatic congestion was observed.

Histologically, in the lungs extensive areas of atelectasis were found, in which there were small groups of emphysematous alveoli. All blood vessels and capillaries were considerably dilated and congested. Perivascular edema and erythrocytes were noted in the collapsed alveolar spaces. In the small bronchi the lumen was narrowed, and their mucosa was collected in the form of tall folds. There was mucus in the bronchial tubes. In the myocardium as well as in the liver, kidneys and spleen pronounced dilatation and congestion of the blood vessels was found. In the brain there were moderate signs of hypostatic congestion of the pia mater and brain tissue with slight perivascular edema and small hemorrhages (Figure 6).

Similar changes were observed in other animals of this group, and thereby the pulmonary involvement in them was also distinct.

The second group was made up of four dogs whose vagus nerves were cut — in two, during inhalation of compressed oxygen, and in two, before the oxygen effect.

As an example gross and microscopic autopsy findings are given for dog No. 22, which was vagotomized before the experiment and died 87 min after the beginning of the compressed oxygen effect.

On autopsy, small areas of atelectasis were found in the posterior lobes of the lungs (one on the right and two on the left). In the epicardium

occasional punctate hemorrhages were found. The chambers of the right heart and left atrium were dilated and filled with blood; the left ventricle was contracted. In the liver, lungs, spleen and intestine there was pronounced venous congestion. Histologically, small areas of atelectasis were noted in the lung tissue. The veins and capillaries were dilated and filled with blood. Around the large blood vessels there was edema of the areolar connective tissue. In the myocardium, liver, kidneys and spleen, hypostatic congestion was found.

Therefore, in this dog, as in the second one, exposure to the effect of compressed oxygen for 31 min, resulted in less pronounced atelectasis than in animals of the control group.

In the other two dogs of this group, the vagus nerves in the neck were cut during the period of development of oxygen convulsions. At autopsy and on histological examination a more marked congestion of the lungs and pulmonary edema were found than in the control animals. In these cases, the more active pulmonary involvement was not connected with the duration of action of compressed oxygen, since the exposure time (in one dog 46 min; in the other, 66 min) did not exceed or was even shorter than in animals of the control group.

The third group was made up of five dogs, in which prior to the action of compressed oxygen the suprarenal glands were isolated by application of a circular ligature, which disconnected their circulation from the general circulation. In addition, in two dogs the ansa subclavia and both splanchnic nerves were cut; in one dog, only the left splanchnic nerve.

The results of the investigations showed that pulmonary involvement in these animals was very slight, whereas hypostatic congestion in the abdominal organs was greater than in dogs of the control group. This was particularly noticeable in cases where isolation of the suprarenal glands was combined with bilateral or unilateral section of the splanchnic nerves.

As an example brief autopsy and histological data are presented on the dog in which the suprarenal glands were isolated and the ansa subclavia and splanchnic nerves were cut. The dog died after the 3 hour effect of compressed oxygen.

At autopsy the posterior lobes of the lungs were moderately congested with small areas of peripheral atelectasis; the anterior and middle lobes were not abnormal. There was pronounced hypostatic congestion in the abdominal organs.

Histological examination revealed small, chiefly subpleural areas of atelectasis intermingled with areas of dilated alveoli. The pulmonary blood vessels, particularly the capillaries, were dilated and congested, chiefly at the sites of atelectasis. There was edema around the large blood vessels. In places, small areas of lung tissue were encountered with edema and hemorrhages into the alveolar lumina. Marked hypostatic congestion was observed in the spleen, liver, kidneys, and myocardium.

Similar pathological changes were found in the other animals of this group. The comparatively slight involvement of the lungs, despite the fact that exposure to high oxygen pressures was approximately 2—3 times longer than with control animals, is striking.

Discussion of Results

The results of autopsy and histological examination of the internal organs of guinea pigs and dogs exposed to the effects of high oxygen pressures showed that in both types of animals pathological changes of a similar nature are found. In dogs, in contrast to guinea pigs, the congestion of the pulmonary blood vessels was more pronounced, and there was no eosinophilic infiltration of the alveolar septa or peribronchial tissue.

The pathological changes which we found are similar in nature to those described in animals exposed to the long-term effect of oxygen under ordinary barometric pressure. They differ from the latter in that the lungs are less intensely involved and show no appreciable inflammatory reaction. However, this fact does not exclude the possibility of pneumonia developing from the long-term effect of high oxygen pressure.

In guinea pigs which had first been atropinized, eosinophilic infiltration in the lungs is encountered less often. The somewhat lesser intensity of pulmonary involvement in some of them does not go beyond the limits of individual variations which are found in the group of control animals. Other authors (Grognot and Chome, 1955, and others) have also noticed such individual characteristics in the development of pathological reactions to oxygen in the same species of animal.

In vagotomized dogs exposed to the effect of high oxygen pressures, a definite reduction of pathological changes in the lungs is noted (2 experiments), whereas in experiments on guinea pigs preliminary atropinization had no effect on the course of the pathological process in the lungs. From this data it follows that it is not so much the sensory innervation of the lungs as the effect on the vagal fibers which is significant in the development of pulmonary lesion in acute oxygen poisoning.

This agrees with studies made by Bykov, Rikkl', Chernigovskii, and Potapova (1943), who showed that after cutting the vagus nerves in the necks of rabbits, adrenalin-induced pulmonary edema does not occur or, if [in exceptional cases] the animal does die of pulmonary edema, it develops later and is less pronounced than in intact animals. Preliminary atropinization of the rabbits does not exert a favorable effect in this case.

In our experiments the greatest effect on the course of acute oxygen poisoning and the resulting pathological changes is exerted by isolation of the suprarenal glands, particularly when combined with cutting the splanchnic nerves. In all animals in which this was done, first of all, slight involvement of the lungs is found, despite the fact that exposure to the effect of high oxygen pressures is 2—3 times longer than that of the control animals; secondly, the lifespans of these animals under conditions of compressed oxygen are longer than those of the control animals.

The data obtained attests to the significance of humoral factors in the development of pulmonary lesions in acute oxygen poisoning. Of importance in this connection are the studies made by Tonkikh (1944) dealing with determination of the origin of pneumonias when the superior cervical sympathetic ganglia are stimulated. It has been determined that pathological influences on the lungs are realized not only through the nervous system but also through participation of humoral factors. The significance of the

latter is evident, first of all, from experiments on hypophysectomized animals, in which, following stimulation of the superior cervical sympathetic ganglia no pneumonia develops (Moiseev and Tonkikh, 1945); and secondly, by cross-circulation experiments, in which stimulation of the neural structures of one dog led to the development of pneumonia not only in it but also in the other dog (Bekauri, Tonkikh, and Shenger, 1946).

There is reason to believe that the neurohumoral mechanism of development of pulmonary lesions also takes place in acute oxygen poisoning. This is attested to by the observations of a number of authors as well as our own experiments with isolations of the suprarenal glands.

Bean (1952) showed that preliminary removal of the hypophysis in mice exposed to the repeated effects of high oxygen pressures (5—6 atm) is accompanied by a less pronounced pulmonary involvement than in the control animals. The effect is eliminated by the injection of adrenocorticotropic hormone (ACTH) into the hypophysectomized animals.

Grandpierre and Grognot (1954) observed that the administration of ACTH or extracts from the suprarenal cortex increases the intensity of pulmonary involvement under the influence of oxygen.

Gershman, Gilbert, Nye, Price, and Fenn (1955) have shown that after removal of the suprarenal glands in mice, the lethal effect of high oxygen pressures is delayed. According to their data, a more favorable effect is exerted by complete removal of the suprarenal glands than by demedullation of them. The effectiveness of removal of the suprarenal glands is considerably reduced by the injection of epinephrine, and is completely eliminated by the administration of cortisone or an extract of the suprarenal cortex.

The above data permits us to assume that the effect of high oxygen pressures is accompanied by excessive stimulation of the hypophyseal-suprarenal cortical system. That isolation of the suprarenal glands favorably effects development of pathological pulmonary changes and increases the lifespans of these animals under conditions of compressed oxygen is probably explained by the fact that in these cases the adrenocorticotropic reaction is not realized.

When isolation of the suprarenal glands is combined with cutting of the splanchnic nerves, the intensity of pulmonary involvement from the effect of high oxygen pressures is particularly slight. This, apparently, is associated with the fact that the procedure on the splanchnic nerves leads to congestion of the abdominal organs. The considerable reduction in the quantity of circulating blood causes a reduction of pulmonary stasis and edema.

Conclusions

1. Pathological changes in the lungs occurring under the influence of high oxygen pressures took the following forms: dilatation and congestion of the veins and capillaries, sometimes with hemorrhages into the surrounding tissues and alveoli; perivascular edema; thickening of the alveolar septa due to edema and dilatation of the capillary system; development of different degrees and magnitudes of atelectasis. Pulmonary involvement was associated with a more or less pronounced congestion of other internal organs.

2. Isolation of the suprarenal glands in dogs, particularly in combination with cutting of the splanchnic nerves, is accompanied by less pronounced pathological changes in the lungs under the influence of high oxygen pressures. This fact emphasizes the importance of humoral factors in the development of pulmonary involvement in acute oxygen poisoning.

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N66-17142

P. A. Sorokin

CHANGES IN THE ELECTRICAL ACTIVITY OF THE HEARTS OF ANIMALS UNDER THE INFLUENCE OF HIGH OXYGEN PRESSURE

(Izmeneniya elektricheskoi aktivnosti serdtsa u zhivotnykh pri deistvii vysokikh davlenii kisloroda)

Under the influence of high oxygen pressures serious disorders of various body functions, including those of the cardiovascular system, occur comparatively quickly.

Whitehorn and Bean (1952) report electrical activity changes in the hearts of decerebrate dogs under the long-term effect of high oxygen pressure (5 atm). Under these conditions they observed bradycardia and a delay in AV conduction. At the same time, ventricular extrasystoles and an AV (nodal) rhythm were sometimes found. These changes occurred in the early period of the compressed oxygen effect and were eliminated by cutting the vagus nerve. However, this procedure, according to their data, did not prevent the development of bradycardia or heart block in the late periods of oxygen poisoning.

It should be noted that decerebration, being in itself a very serious and traumatizing procedure, exerts a marked influence on the circulatory system. Therefore, it seemed advisable to us to study the electrical activity of the heart in intact animals in the developmental dynamics of acute oxygen poisoning.

Method

The first series of experiments was performed on intact guinea pigs. The animals were bound by their legs on a special stand in a supine position. To record an electrocardiogram (ECG) we used needle electrodes which were inserted into the subcutaneous tissue and fastened with a strip of adhesive tape. The guinea pig was placed in a steel chamber 65 l in volume, inside which the electrodes were attached to leads going to the electrocardiograph. The chamber was closed; after 2 or 3 min oxygen was blown in for the purpose of removing the air.

The first group of experiments was performed under a pressure of 1, 2, and 3 atm, with exposure times of 150—180 min (27 experiments). The ECG tracing was made with three standard leads and, in various experiments, with the use of a fourth lead also (right foreleg and apex of heart).

First, an ECG was recorded in the initial position (15 min after tying the guinea pig to the stand); then, at the beginning of the oxygen effect; subsequently, every hour and at the end of the experiment.

For the purpose of studying the electrical activity of the heart in the convulsive forms of acute oxygen poisoning the experiments were performed under a pressure of 5.5 atm (16 experiments). The ECG tracings were made in the initial position, then every 10 min during the action of compressed oxygen until convulsions developed and following decompression during the aftereffect period. In various experiments electrocardiographic observations were made until the animal died. In eight experiments the guinea pigs were given a subcutaneous injection of an atropine solution in a dose of 1 mg/kg prior to the effect of compressed oxygen (5.5 atm).

The oxygen content of the chamber ranged from 92—96%; the carbon dioxide content, from 0.05—0.2%.

As controls, the basic data as well as the results of 14 control experiments performed under conditions of breathing oxygen at a pressure of 1 atm were used.

The second series of experiments was performed on dogs anesthetized with urethane. In all, 15 experiments were performed; of these, 6 were on intact animals; 7 on animals vagotomized prior to the effect of oxygen or during the occurrence of oxygen-induced convulsions; 2, on animals in which the heart was denervated in the convulsive period of acute oxygen poisoning.

The experiments were performed in a large compression chamber. All the experimental animals were exposed to the action of oxygen under a pressure of 6 atm. The nitrogen content in the oxygen supply for breathing did not exceed 2%. An ECG was recorded in the initial state and from time to time at various phases of acute oxygen poisoning.

Results of the Investigations

First Series of Experiments. In the initial state the number of heart beats per min in guinea pigs ranged from 214 to 350 (an average of 285). The PR interval was from 0.04 to 0.09 sec (an average of 0.06); the QRS, from 0.025—0.04 sec (an average of 0.03); QT, 0.09—0.16 sec (an average of 0.13). As far as the shape of the waves in the normal guinea pig ECG is concerned, the P wave was always positive with a rounded and, rarely, pointed peak. The Q wave was rarely encountered and only in the first lead. The R wave was always directed upward and was largest in the second and, rarely, in the first lead. The S wave was found in about half of the experiments, always in the third lead. The T wave in the first lead was usually negative, rarely positive, or not differentiated at all; in the second lead in two-thirds of the investigations it was directed upward; in one-third, downward. In the third lead the T wave was positive as a rule.

The PR and R(S)T segments in the second and third leads were displaced downward 0.5—1.0 mm from the isoelectric line.

In experiments with oxygen pressures of 1.0 and 2.0 atm, for 2.5—3 hrs (24 experiments) no appreciable abnormalities were noted in the behavior of the guinea pigs. The electrocardiogram was normal in 14 experiments; in 10 a distinct reduction of the T wave was observed (Figure 1).

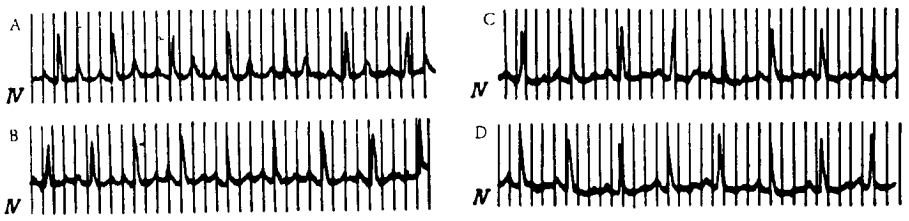


FIGURE 1. Changes in the fourth lead of the electrocardiogram of guinea pig under the influence of oxygen at a pressure of 1 atm (experiment of 12 July 1955)

A—basic ECG (sinus rhythm, 240 beats/min); B—ECG 1 hr after the animal had been put in an atmosphere of oxygen; C—ECG, 2 hrs after; D—ECG 2.5 hrs after (a certain increase in the heart rate occurred—about 300 per min—and there is some flattening of the T wave).

During the effect of oxygen under a pressure of 3 atm (three experiments) motor restlessness was noted, but without development of convulsive phenomena. In one guinea pig, at the end of the experiment with oxygen the number of heart beats dropped from 320 to 120/min; various impulses came from the AV node during the aftereffect. The guinea pig was lethargic and did not eat for a day. Under the influence of oxygen at 5.5 atm local spasms appeared in the intact guinea pigs after 13—38 min (on the average, after 22.6 min); generalized convulsions appeared after 18—46 min (on the average, after 32.2 min). In most observations changes in electrical activity of the heart were found before the development of convulsive phenomena and were characterized by reduction of the heart rate (on the average, by 24%). Slowing of the heart beats occurred because of a change in the sinus rhythm (five experiments), SA block (two experiments), or incomplete heart block (one experiment). In the convulsive period heart block was observed more often (seven experiments); nodal and idioventricular rhythms (four experiments), less often. The changes indicated above were accompanied by slow ventricular contractions (50—100/min), reduced size of the T waves and increase in heights of the R waves. At the beginning of the oxygen effect the T waves increased in size somewhat; in the convulsive period, they gradually decreased in size, and, not uncommonly, in those cases where they had been positive, became negative. At the same time, during the convulsions, the R(S)T segment was gradually displaced downward, reaching its most pronounced degree during the development of terminal signs. After the oxygen effect had stopped, if the animal survived, normalization of the electrocardiogram occurred.

As an illustration we are presenting electrocardiographic data for guinea pig No. 25 (Figure 2). In this case, even at the beginning of oxygen poisoning incomplete heart block developed, which, with increase in oxygen poisoning (convulsions and respiratory depression), was accompanied by progressively more frequent omissions of the ventricular contractions and a progressive downward displacement of the R(S)T segment (Figure 2, B—E). After the oxygen effect had stopped the electrocardiographic tracing was the same as the original (Figure 2, G).

In the initial period of the toxic oxygen effect, along with a slowing of the heart rate ventricular extrasystoles (Figure 2, B) not uncommonly were observed.

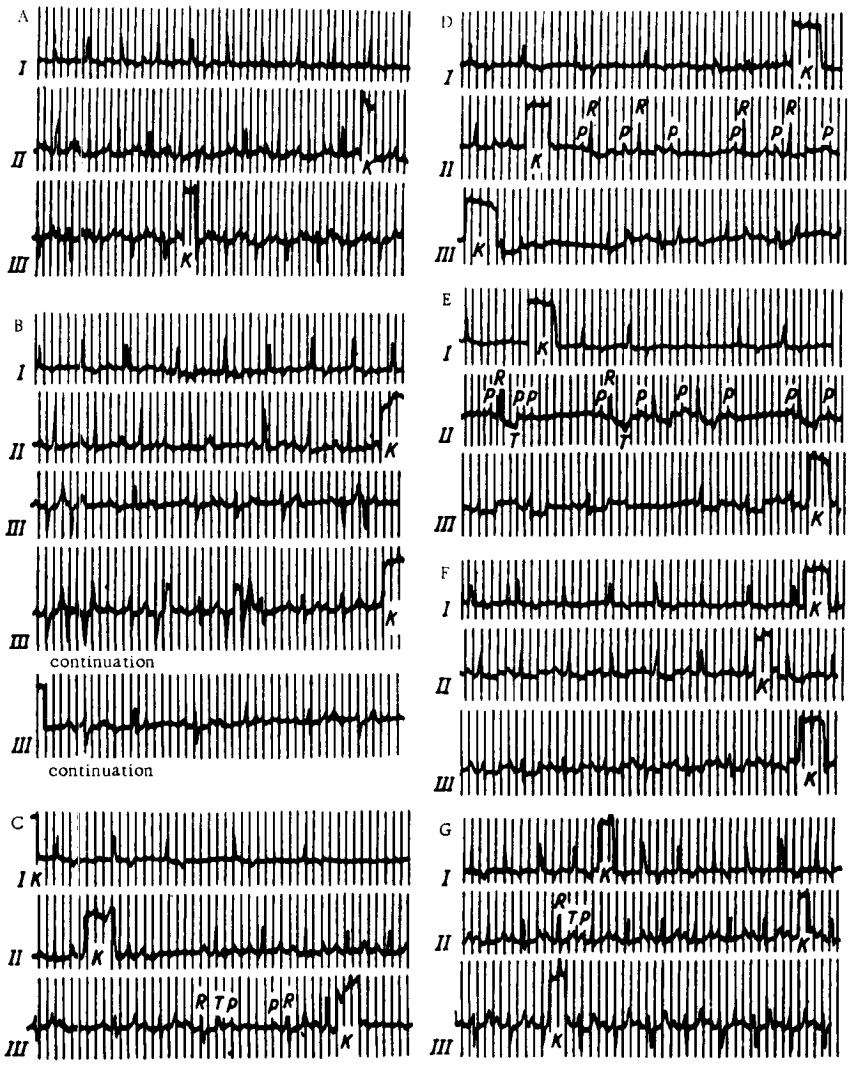


FIGURE 2. Changes in the electrical activity of the heart of guinea pig No. 25 under the influence of oxygen at a pressure of 5.5 atm (experiment of 2 October 1955)

A — basic ECG (sinus rhythm, 280 beats/min); B — ECG 10 min after the beginning of the oxygen effect (190 ventricular contractions/min; incomplete AV block; ventricular extrasystoles; increase in the size of the R waves); C — ECG after 35 min; convulsive period (heart rate, 150/min; as before, incomplete heart block; the T wave increased in size in the 2nd and 3rd minute). D — ECG after 50 min; convulsive period (cardiac contractions 130/min; ST segment begins to be displaced downward from the isoelectric line; flattening of the T waves; otherwise the data are the same as on the previous ECG); E — ECG after 65 min; rate convulsions; respiratory depression (cardiac contractions, about 100/min; as before, incomplete AV block; the ST segment is displaced downward even further; T waves are negative); F — ECG 10 min after decompression and discontinuance of the oxygen effect (sinus rhythm, 220 beats/min, ST segment displaced downward less than on previous ECG; the T waves are flattened); G — ECG 68 min after decompression (sinus rhythm about 280/min; ECG is the same as the original). K — control, 1 mV = 1 cm. Time marking — 0.05-second intervals.

In guinea pigs which had been injected subcutaneously with atropine prior to the effect of compressed oxygen no slowing of the heart rate was observed. No other cardiac arrhythmias characteristic of acute oxygen poisoning in intact animals were observed here either. As an illustration of what has been stated the data of three experiments pertaining to the same guinea pig are presented (Figure 3).

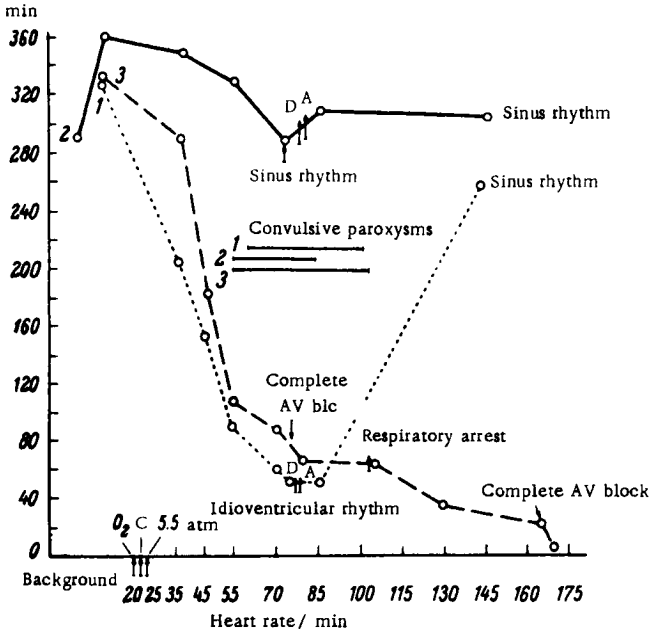


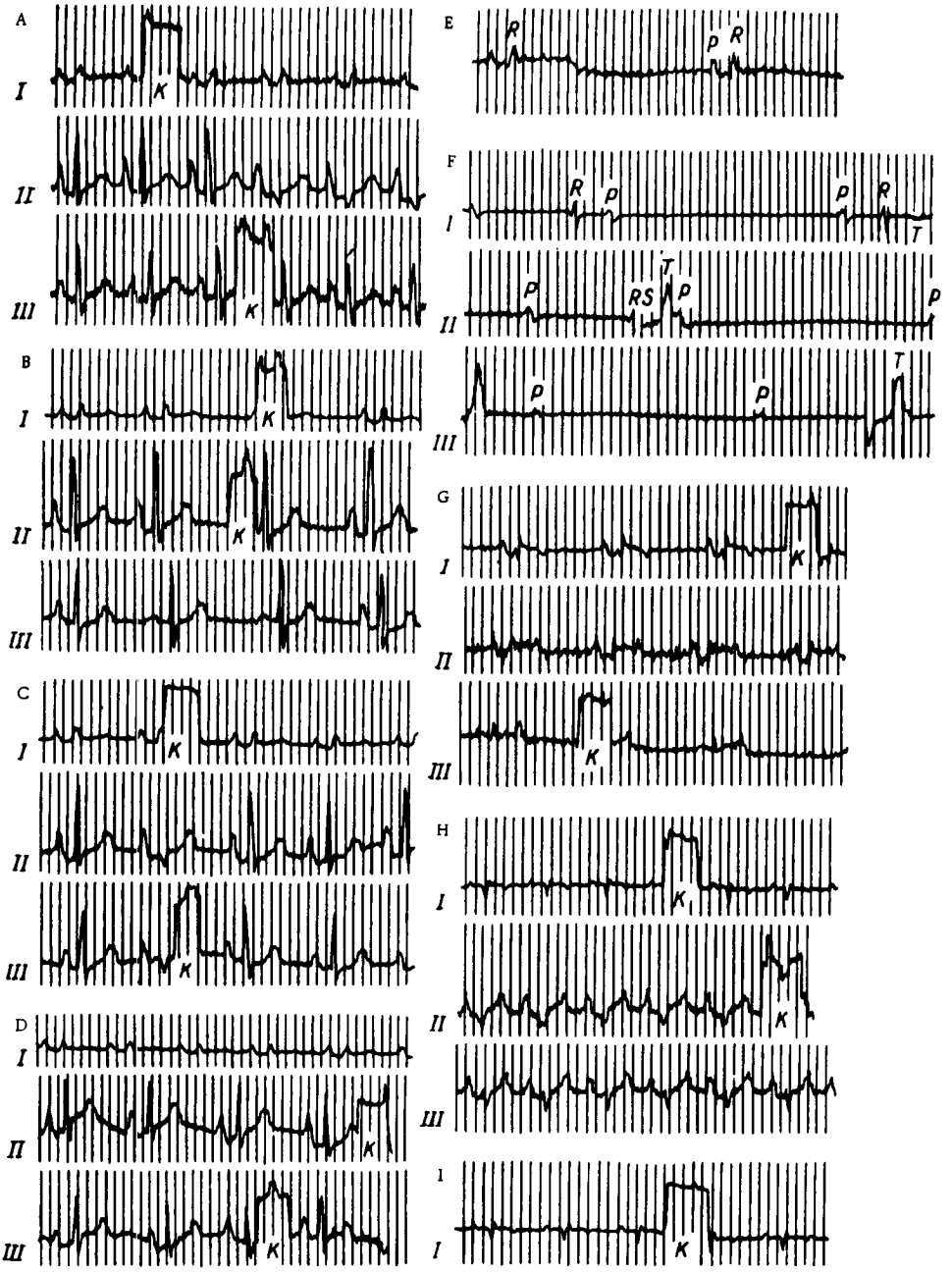
FIGURE 3. Curves of the heart rate of guinea pig No. 23 under the influence of oxygen at a pressure of 5.5 atm (data of three experiments), 28 September (1) 5 October (2) and 17 December (3)

On the abscissa, the number of heart beats/min; on the ordinate, the time (in min). AV — atrioventricular block; O_2 — beginning of breathing of oxygen; C — compression; D — decompression; A — inhalation of air.

Second Series of Experiments. The changes in the electrical activity of the heart in anesthetized dogs depended on the phases of development of acute oxygen poisoning. The initial reaction to high oxygen pressures is a certain reduction in the heart rate. As soon as hyperpnea developed in the animals, tachycardia developed, continuing even during convulsive

FIGURE 4. Change in the electrical activity of the heart in an anesthetized dog under the influence of an oxygen pressure of 6 atm (experiment of 2 February 1957)

A—initial ECG (sinus rhythm, about 160/min); B—ECG 5 min after the action of compressed oxygen (sinus rhythm, about 110 beats/min); C—ECG after 15 min, during oxygen-induced hyperpnea (the same data, heart rate about 130/min); D—ECG after 22 min, at the beginning of the convulsive period (data is the same as on the previous ECG); E—ECG after 33 min; convulsive period (sinus rhythm about 48 beats/min); F—ECG after 53 min; convulsive period—AV block with a heart rate of about 30/min); G—ECG after 60 min—beginning of terminal period (sinus rhythm, heart rate about 110/min; the waves are considerably reduced in size; the T waves in the second and third leads are relatively large and in the first lead, negative; elevation of the ST segment); H—ECG after 66 min; terminal period (sinus tachycardia, about 185 beats/min; Q is deep in the first lead; the R waves are markedly reduced in height; the P and T waves are relatively large in the second and third leads; there is considerable elevation of the ST segment); I—ECG recorded during decompression, 14 min after respiratory arrest (data is the same as on the previous ECG).


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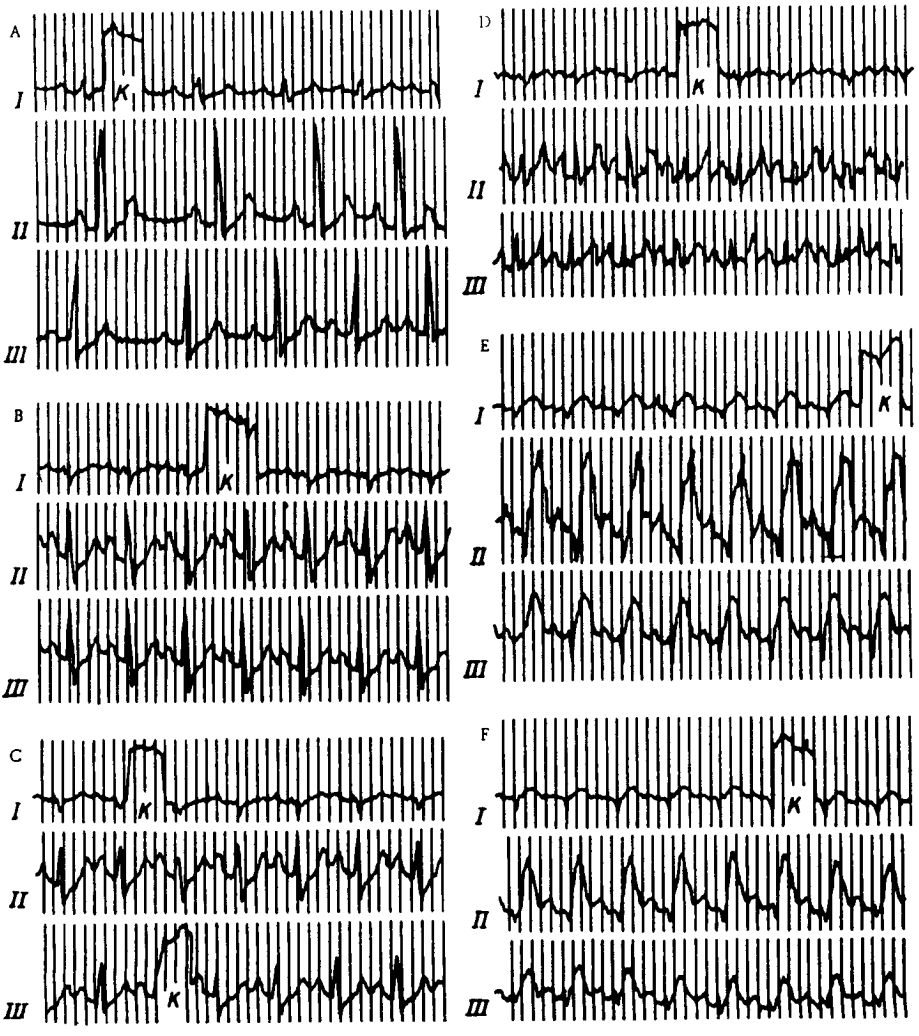


FIGURE 5. Electrocardiographic changes in a vagotomized dog under the influence of compressed oxygen (6 atm). Experiment of 24 January 1957

A — basic ECG (sinus rhythm, about 120/min); B — ECG 6 min after vagotomy, breathing of air (sinus rhythm, 220 beats/min); C — ECG 10 min after the action of compressed oxygen, at the beginning of hyperventilation (sinus rhythm, the changes are the same as on the previous ECG); D — ECG after 35 min, recorded during the convulsions (as before, sinus rhythm, about 230/ min, lowering of the R waves and considerable enlargement of the T waves); E — ECG after 45 min (the same rhythm, 240/min, a marked lowering of the R waves, "giant" T waves, elevation of ST); F — ECG after 56 min, immediately after respiratory arrest, "terminal" period of acute oxygen poisoning (the changes are the same as on the previous ECG).

paroxysms. In the subsequent course of the convulsive period between the paroxysms bradycardia developed, and during actual paroxysm was replaced by tachycardia. At the end of the period of convulsions AV rhythm or heart block occurred; these cardiac arrhythmias were again replaced by sinus tachycardia in the terminal period. After respiratory arrest the heart rate gradually decreased, and "terminal" AV block developed.

Data of electrocardiographic studies of an intact dog anesthetized with urethane is shown in Figure 4. At the beginning of the oxygen effect the heart showed a sinus rhythm, but the heart rate was considerably reduced (Figure 4, B). Beginning with the onset of hyperpnea and at the beginning of the period of convulsions the heart rate again increased (Figure 4, C, D). At the height of the "convulsive" period sinus bradycardia occurred between the paroxysms (Figure 4, E), ending in the development of heart block (Figure 4, F). At the beginning of the "terminal" period sinus rhythm was restored, and a considerable tachycardia began soon after (Figure 4, G, H). In the "terminal" period of acute oxygen poisoning, together with the cardiac arrhythmias indicated above, a considerable reduction of the voltage of the R waves, a deepening of the Q wave in the first lead, and elevation of the RST segment in all standard leads were noted.

Cutting the vagus nerves in dogs eliminates the slowing of the heart rate under the influence of high oxygen pressures. In these animals neither AV rhythm nor heart block is observed during the convulsions (Figure 5). However, cutting the vagus nerves does not prevent the development of AV block in the "terminal" period of acute oxygen poisoning.

It should be noted that in vagotomized dogs exposed to the action of high oxygen pressures, the voltage of the R waves is reduced much more rapidly, and "giant" T waves appear much more quickly (Figure 5, D—F) than in the intact animals, indicating the earlier development of myocardial hypoxia in vagotomized animals.

An additional operation in the form of bilateral section of the ansa subclavia exerts no appreciable effect on tachycardia either during the convulsions or at the beginning of the "terminal" period of acute oxygen poisoning.

Discussion of Results

The results of the studies showed than in intact animals even at the beginning of the action of high oxygen pressures a distinct reduction of the heart rate occurs. In guinea pigs ventricular extrasystoles, SA block, and an AV conduction disorder occur not uncommonly during this period. These cardiac arrhythmias frequently precede the convulsions, being, therefore, early signs of acute oxygen poisoning.

In dogs, in contrast to guinea pigs, the initial moderate slowing of the heart rate is replaced by tachycardia against the background of hyperpnea. With the appearance of clonic and tonic convulsions in the animals bradycardia gradually occurs. This is associated with the development of AV block (complete or incomplete) or nodal or sometimes idioventricular rhythm.

As is well known from the literature, such cardiac arrhythmias are encountered in animals after stimulation of the peripheral end of the vagus

nerves (Smirnov, 1947) or its central structures (Shidlovskii and Kyandzhuntseva, 1953) as well as after administration of acetylcholine (Shidlovskii and Kyandzhuntseva, 1953) or carbocholine (Chumburidze, 1955). In view of this data, as well as the fact that in our experiments with compressed oxygen preliminary atropinization of the guinea pigs or vagotomy in dogs inevitably eliminated bradycardia, heart block or heterotopic rhythm, the connection between these disorders and stimulation of the vagus nerve becomes obvious.

The most frequent cardiac arrhythmia in the convulsive period of oxygen poisoning is AV block. The nature of the conduction disorder in the AV bundle can be understood from the standpoint of Vvedenskii's study of parabiosis (1886, 1901), which was subsequently developed and supplemented by his disciples under the direction of Ukhtomskii (1927, 1930, 1934).

Samoilov (1929) was the first to point out the connection between delayed AV conduction and the phenomena of parabiosis. Subsequently, many authors presented proof of the parabiotic nature of heart block (Borisova and Rusinov, 1940; Chernogorov, 1948; Rafiki, 1954; Isakov, 1958; and others). In addition, SA block is regarded as a manifestation of pessimal inhibition (Arshavskii, 1948).

The study by Vvedenskii and Ukhtomskii gives reason to suppose that under the influence of high oxygen pressures there is a change in the functional condition of the excitable cardiac tissues. In these cases, apparently, stimulation of the vagus nerve and, possibly, also a local effect of high oxygen tensions, results in a reduction of the functional mobility (lability) of the excitable cardiac tissue, contributing to the development of pessimal inhibition. This probably causes both the SA block and the AV conduction disorders.

The change in the terminal components of the ventricular complex is interesting. In guinea pigs a downward displacement of the R(S)T segment from the isoelectric line is noted with simultaneous flattening or inversion of the T wave. These changes usually appear during the convulsions and increase with progression of acute oxygen poisoning, becoming most intense in the terminal period.

In dogs, on the other hand, an elevation of the R(S)T segment is observed, and there is an increase in the size of the T waves, which not uncommonly become "giant" waves. The R wave becomes markedly smaller. These changes usually occur in the terminal period of acute oxygen poisoning. It should be noted that similar changes on the ECG are found in experiments on animals with mild cardiohypoxia caused by bleeding, the administration of sodium nitrate or potassium cyanide (Ar'ev, Kartseva, and Vorob'eva, 1940, 1941; Ar'ev and Kartseva, 1947). "Giant" T waves were recorded also in dogs after compression or ligation of the coronary arteries (Zhil'tsov, 1956; Lengyel, Caramelli, Monfort and Clemente-Guerra, 1957; Egurnov, 1958). The data presented gives us reason to suppose that myocardial hypoxia develops in animals during oxygen poisoning.

The question arises of the cause of this condition in hyperoxemia. The idea that myocardial hypoxia is connected with pulmonary involvement is hardly substantiated, since the pathological changes found in the lung tissue under the influence of high oxygen pressures, although constant, are never so widespread as to produce hypoxemia (Groshikov and Sorokin, 1963). It is more likely that tissue hypoxia develops during acute oxygen poisoning

as a result of a depression of intracellular enzyme oxidation (Bean and Haldi, 1932; Lehmann, 1935; Massart, 1936).

The fact that sinus tachycardia which replaces the heart block and thereby signifies a change to the "terminal" period of acute oxygen poisoning, is not eliminated by cutting the ansae subclaviae, indicates that terminal tachycardia is connected with the action of humoral factors.

In the subsequent course of the "terminal" period, when respiratory arrest occurs, tachycardia is again replaced by bradycardia and heart block. Neither ligation of the vagus nerve nor atropinization eliminates the latter. Therefore, it must be supposed that AV block in this period is brought about by deep- seated metabolic disorders in the heart muscle, resulting from the animal's dying.

Conclusion

1. Changes in electrical activity of the heart in intact animals in the initial period of acute oxygen poisoning are characterized by a distinct slowing of the sinus rhythm and not uncommonly by extrasystoles, as well as by SA block and an AV conduction disorder (in guinea pigs); in the convulsive period, by heart block, and, less often, by nodal or idioventricular rhythm; in the "terminal" period, by sinus tachycardia (in dogs), which after respiratory arrest is again replaced by bradycardia and complete AV block.

2. Preliminary atropinization or cutting of the vagus nerves eliminates slowing of the heart rate, SA block and AV conduction disorder both in the initial and convulsive periods of acute oxygen poisoning, but does not prevent the development of "terminal" bradycardia or heart block.

3. Sinus tachycardia at the beginning of the "terminal" period, which occurs after heart block or heterotopic rhythm, is not eliminated by cutting the sympathetic pathways to the heart.

4. Displacement of the R(S)T segment with negative "giant" T waves and simultaneous lowering of R wave voltage should be regarded as an expression of myocardial hypoxia, which apparently develops because of a depression of tissue respiration during acute oxygen poisoning.

5. Cardiac arrhythmias and other changes in the electrical activity of the heart occurring during the convulsive period of acute oxygen poisoning are transitory and disappear comparatively quickly when the effect of high oxygen pressures is discontinued.

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CHANGE IN THE CIRCULATING BLOOD VOLUME IN DOGS BREATHING OXYGEN UNDER PRESSURES OF 1.0 AND 2.0 ATMOSPHERES

(Izmenenie kolichestva tsirkuliruyushchei krovi u sobak pri dykhanii kislorodom pod davleniem 1.0 i 2.0 ata)

A number of authors have observed that inhalation of increased oxygen concentrations at ordinary atmospheric pressure is associated with a reduction of the minute volume of blood (Anthony, 1947; Keys, Stapp, and Violante, 1943; Whitehorn, Edelman, and Hitchcock, 1946; Sorokin, 1958). This reduction is associated not only with a slowing of the heart rate but also with a reduction of the stroke volume (Whitehorn, et al., 1946).

One of the parameters determining the minute volume of blood is the circulating blood volume. When a reduction of the stroke volume of the heart is observed in hyperoxia a reduction of the mass of circulating blood might also be suspected. However, Hitzenberger and Molenaar (1934) report a certain increase in the circulating blood volume in healthy persons breathing oxygen at ordinary barometric pressure. They believe that the reduction in hemoglobin and red cell count which they observed in these experiments, is explained by the fact that the blood was diluted with tissue fluid.

The need for clarification of what is involved in circulating blood volume, particularly under increased oxygen pressures, led to the present study.

Method

The experiments were performed in a compression chamber, under conditions which remained unchanged, except for the pressure in the chamber and the oxygen content in the gas mixture breathed.

The experimental animals (dogs) were trained to breathe through a mask while lying on their left side. The inlet valve of the mask was connected to a rubberized fabric bag with a corrugated rubber breathing hose. From time to time the bag was filled with oxygen through a tube from the tank located outside the chamber. The outlet valve was similarly connected with another bag, which held the exhaled air. As the bag was filled the latter was directed out into the outside air.

To prevent the possible development of conditioned reflexes to the experimental situation, the experiments usually were performed once a week, and there were two intervals totaling 14 days. In this connection, control studies were made both at the beginning and end of the observation series.

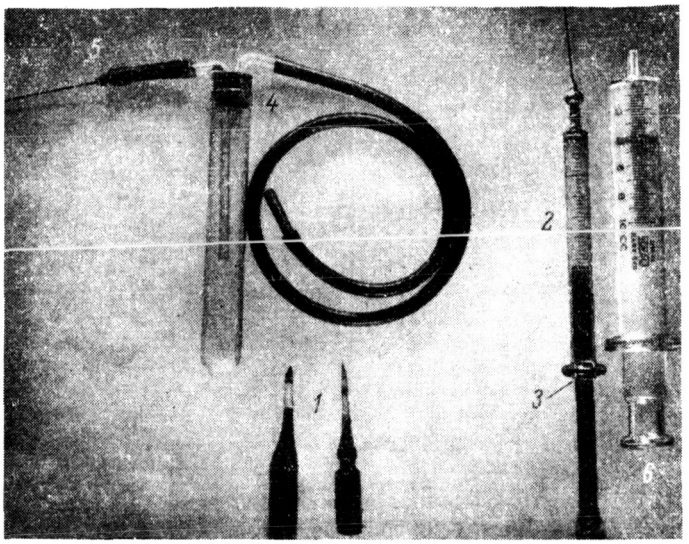


FIGURE 1. Apparatus for taking blood and syringe for injecting dye solution into the vein

1 — ampules containing T-1824 dye solution; 2 — tuberculin syringe for intravenous injection of the dye solution; 3 — adapter; 4 — system for taking blood; 5 — needle with rubber tube for taking blood; 6 — 10-ml syringe.

On the day of the experiment the dogs were weighed, fitted with breathing masks, placed on their left side, and allowed to breath ordinary air (control) or oxygen under pressure of 1.0 and 2.0 atm. The circulating blood volume was investigated 3—4.5 hrs after the beginning of the experiment.

The determination of the circulating blood volume was made with Evan's blue (T- 1824)* according to the method described by Gregersen (1944). Initially, a standard solution (0.5—1.0%) in physiological saline or distilled water was prepared from the dye T—1824. In our experiments a 0.48% solution of the dye in distilled water was used.

From this standard dye solution a solution was prepared in distilled water in a 1:50 ratio, and then a solution in a dilution of 1:500 was prepared by mixing 0.2 ml of the 1:50 dye solution with 1.8 ml of dog's plasma.

The control solution was prepared by mixing 0.2 ml of distilled water with 1.8 ml of the same plasma used for the preparation of the standard solution.

The standard and control solutions were poured into cuvettes, to a depth of 10 mm. We made use of specially prepared cuvettes with a capacity of 1.5 ml. The optical density of the standard dye solution was determined with a spectrophotometer (SF-4) for a wavelength of 624 mμ. Through repeated studies the optical density of the standard dye solution (D) was determined and found to be equal to 0.690.

* I should like to take this opportunity to thank F. Yu. Rachinskii and D. V. Ioffe, workers in the Department of Organic Chemistry of the Kirov Military Medical Academy, who, at our request, prepared the T-1824 dye.

For intravenous injection of the dye solution we used a tuberculin syringe (Figure 1, No. 2) furnished with a special adapter (Figure 1, No. 3) which was attached to the upper portion of the syringe barrel. The adapter, a wire curved in the form of a rectangle, is clamped to the plunger of the syringe and, when the syringe is filled with 1 ml of the dye solution, coincides with a circular depression on the plunger. This adaptation was necessary, because when the syringe is filled with the dye solution it is impossible to see either the division on it or the base of the plunger. The adapter made possible injections which always contained about the same amount of dye; error was no greater than ± 0.3%.

The quantity of solution injected into the vein was determined from the formula $V=\frac{P}{D}$, where V is the volume of dye solution injected; P is the weight of the volume of dye injected into the vein; D is the specific gravity of the dye solution, equal to 1.00022. By substituting the appropriate figures, we obtain $V = \frac{1.021}{1.00022} = 1.019$ ml (which amounts to 4.89 mg of the dry dye).

Usually, the blood taken from the dogs was from the right jugular vein and the left common carotid artery, which were first exteriorized separately in a skin flap. The first blood sample, serving as a control, was drawn from the jugular vein into a test tube in a quantity of 4—5 ml. Without being removed from the vein, the needle, along with the rubber tube attached to it, was disconnected from the test tube (Figure 1, No. 5; 2, No. 1); then a 10 ml syringe containing physiological saline solution was connected to the rubber tube (Figure 1, No. 6; 2, No. 2). By means of a puncture in the rubber tube, 1 ml of 0.48% dye solution was injected into the vein from the tuberculin syringe, and the remainder of the dye solution was forced into a container by the physiological solution from the rubber tube and the needle (Figure 2). After 10 min (the time needed for fixing of the dye solution with the circulating blood) a second blood sample, also in a quantity of 4—5 ml, was taken from the jugular vein or carotid artery of the opposite side.

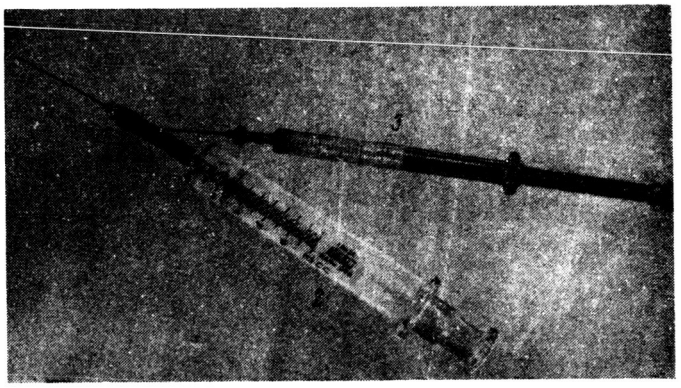


FIGURE 2. The position of the tuberculin syringe at the time of injection of the T-1824 dye solution into the vein

1 — needle with rubber tube; 2 — 10-ml syringe containing physiological saline solution; 3 — tuberculin syringe for intravenous injection of the T-1824 dye solution.

The relationship between the plasma and red cell volumes was determined by the copper sulfate method proposed by Philips and co-authors (Philips, van Slyke, Dole, Emerson, Archibald, and Hamilton, 1943). For this purpose, in the control sample a determination was made of the specific gravity of whole blood and then of the plasma obtained by centrifugation. This metatocrit (*Hct*) is calculated from the following formula:

$$Hct = \frac{(\text{sp. gr. of blood}) - (\text{sp. gr. of plasma})}{1.104 - (\text{sp. gr. of plasma})},$$

where 1.104 is the specific gravity of the dogs' red cells. A nomogram may be used for the same purpose.

The blood samples were examined for hemolysis, and in its absence a determination was made of the density of the dye.

The volume of circulating plasma (*PV*) was calculated from the following formula:

$$PV = \frac{D_1 \times 500 \times V}{D_2}, \qquad (1)$$

where D_2 is the optical density of the dye in the circulating plasma after mixing; D_1 is the optical density of a standard dye solution diluted 1:500 in the plasma; V is the volume of injected dye solution.

Because the same concentration of injected dye solution (0.48%) was always used in our investigations, the optical density was constant, i.e., equal to 0.690 when the same cuvette was used with solution 10 mm deep. The volume of dye solution (*V*), injected into the vein wals also constant, i.e., equal to 1.019 ml. Substituting these values into formula (1), we determine the quantity of circulating plasma in ml:

$$\frac{0.690 \times 500 \times 1.019}{D_2} = \frac{351.5}{D_2}.$$

The circulating blood volume in ml (*OV*) was calculated from the following formula:

$$OV = \frac{PV}{100 - Hct} \times 100, \qquad (2)$$

where *PV* is the quantity of circulating plasma in ml, as calculated from formula (1).

Results of the Investigations

In 20 control experiments performed when the animals were breathing ordinary air, the volume of circulating plasma was, on the average, 47.3 ml/kg body weight with extremes of 42.2—53.0 ml/kg. The circulating blood volume, on the average, was 84.4 ml/kg. The values obtained in different experimental animals were from 76.0—93.0 ml/kg (Figure 3). However, variations in the circulating blood volume in the same animal were slight and did not exceed 5.0 ml/kg. Therefore, it appears that a more or less constant circulating blood volume is characteristic of each animal under conditions of physical rest.

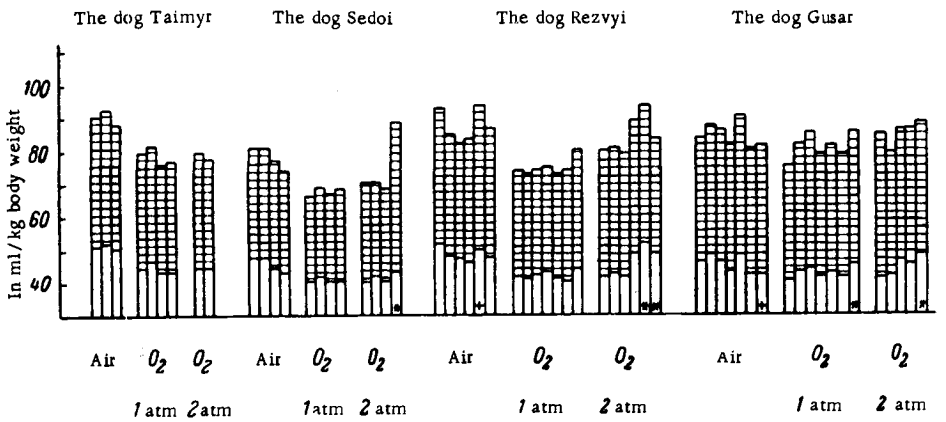


FIGURE 3. Changes in the circulating blood volume in dogs breathing oxygen under pressures of 1.0 and 2.0 atm

Columns — circulating blood volumes (ml); unhatched portion of the columns — quantity of circulating plasma; the asterisks indicate the mass of circulating blood after preliminary subcutaneous injection of an atropine solution; the "+" signs, determinations of the mass of circulating blood during the aftereffect period.

Our results agree with the investigation data of other authors. Thus, Bonnycastle, and Cleghorn (1942) found, using the Evans dye method in 106 dogs, that the circulating plasma volume was within limits of 31.8 and 64.6 ml/kg (on the average, 48.3 ml/kg). The total circulating blood volume ranged from 60.0 to 107.5 ml/kg (on the average, 83.2). The greater variation in the figures for circulating blood in their experiments as compared with our data is striking. This, in our opinion, is explained by the fact that these authors made their investigations on untrained animals, which did not remain quiet enough during the blood-taking procedure.

During the breathing of oxygen under ordinary atmospheric pressure the quantity of circulating plasma was from 39.1 to 44.0 ml/kg (averaging 41.8 ml/kg). In 18 out of 21 determinations a reduction in this figure, by an average of 12%, was noted. In only one dog, in 3 out of 6 experiments, were the figures obtained the same as for the control. Together with a reduction in the circulating plasma volume there was also a reduction of circulating blood volume. It amounted, on the average, to 75.6 ml/kg with extreme figures of 66.2—83.8 ml/kg. Just as in the control experiments, variations in the quantity of circulating blood were small and did not exceed ± 4.2 ml/kg.

Under an oxygen pressure of 2.0 atm, the quantity of circulating blood plasma in dogs was, on the average, 48.1 ml/kg; the circulating blood volume, 79.7 ml/kg. In 10 out of 13 experiments the circulating plasma volume decreased by 11.6%, on the average, while the mass of circulating blood decreased by 9.4% in nine experiments. Therefore, in these observations the changes in the circulating blood volume were in the same direction as during the breathing of oxygen under ordinary pressure.

After preliminary atropinization of the animals, the circulating blood volume did not change or even increased somewhat from the normal.

During the aftereffect period the figures obtained for the circulating blood were the same as the control figures.

Discussion of Results

Our investigations showed that in animals under the influence of increased oxygen concentrations, a reduction of the circulating plasma and circulating blood volumes usually occurs. The data which we obtained does not agree with the results of investigations made by Hitzenberger and Molenaar (1934), who found a reduction of the hemoglobin and the red cell count, with some simultaneous increase in the circulating blood volume, which they explained by the transudation of tissue fluid into the blood vessels. This discrepancy is apparently explained by the fact that the exposure to oxygen was brief (20 min), whereas in ours it lasted more than 2 hrs.

It is well known that circulating blood mass is closely connected with the function of the so-called blood depots. The spleen is the main organ possessing the ability to retain blood (Botkin, 1874; Barcroft, 1937). Such organs as the liver, lungs, and the subpapillary venous plexus of the skin, where blood may be retained in considerable amounts because of a slowing of the circulation, are now regarded as blood depots.

The functions of blood depots are connected with the activities of the autonomic nervous system. Barcroft (1937) showed that the denervated spleen stops contracting in response to carbon monoxide intoxication. As has been determined, stimulation of the sympathetic nervous system is accompanied by the liberation of blood from the blood depots and an increase in the circulating blood volume (Grab, Janssen, and Rein, 1929; Barcroft, 1937; and others). Stimulation of the parasympathetic system exerts the opposite effect (Teplov, 1941).

It is well known that the emptying of the blood depots is an adaptive reaction to conditions requiring an increased supply of oxygen to the tissues (strenuous activity, blood loss, hypoxemia, etc.). When a state of hyperoxia occurs in the body, a retention of blood in the depots of internal organs is noted, as our data has shown. This is associated with the reduction of the minute volume of the blood during the breathing of oxygen, as has been mentioned above.

Reduction of the circulating blood volume should be regarded as an adaptive reaction to increased oxygen tension. The mechanism of this reaction is apparently closely connected with stimulation of the parasympathetic innervation, as is evidenced by the fact that after preliminary atropinization of the animals no reduction of circulating blood volume was noted. The reduction of this hemodynamic index under conditions of hyperoxia is temporary, because during the aftereffect period the quantity of circulating blood in the experimental dogs is the same as that in the controls.

Conclusions

1. In dogs breathing oxygen at pressures of 1 and 2 atm, a distinct reduction in the circulating blood volume is usually found.
2. Reduction in the circulating blood volume should be regarded as an adaptive reaction to an increased partial oxygen pressure in the inhaled air.

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CHANGE IN THE ADSORPTIVE PROPERTIES OF THE NERVOUS SYSTEM AND INTERNAL ORGANS OF WHITE MICE DURING OXYGEN-INDUCED CONVULSIONS

(Izmenenie sorbtsionnykh svoistv nervnoi sistemy i vnutrennikh organov belykh myshei pri sudorozhnom deistvii kisloroda)

The morphological substrate of functional disorders occurring in the nervous system and internal organs under the influence of increased oxygen pressure has drawn the interest of many investigators. However, comparatively recent pathological studies of animal organs have revealed very slight morphological changes (Dionesov, Kravchinskii, Prikladovitskii, Sonin, 1934; Bean, 1945; Smirenskaya and Romanova, 1958; Zagorskii, 1960; and others).

Methods have now been worked out for the detection of fine cytophysiological changes in tissues under various functional conditions. Intravital staining is one of the methods suitable for this purpose.

Under the influence of various chemical and physical agents, reversible material changes occur in living cells and tissues, a phenomenon which D. N. Nasonov and V. Ya. Aleksandrov (1934) termed paranecrosis. One of the signs of paranecrotic change is an increase in the affinity of living matter for intravital dyes (Nasonov and Aleksandrov, 1940; Nasonov, 1959). This is demonstrable by means of the method of quantitative determination of the adsorbed properties of tissues worked out by A. A. Braun and M. F. Ivanov (1933).

For the study of intravital staining of isolated mammalian organs, V. Ya. Aleksandrov's method (1949) has been used. Recently, intravital staining of organs of intact mammals has been adopted on a broad scale (Mandel'shtam, 1939; Aleksandrov, 1949; Savich, 1952; Grebenskaya, 1958; Gramenitskii and Makhover, 1958; Korchak, 1958; Romanov, 1958; Makhover, 1959).

The method of intravital staining has been successfully used by Z. I. Barbasheva and A. G. Ginetsinskii (1956) for studying adaptation to reduced oxygen pressure.

The object of the present study was to utilize intravital staining of both isolated organs and the intact organism in order to demonstrate the occurrence of fine material changes in the central nervous system and some internal organs under conditions of increased oxygen pressure.

Method

The experiments were performed in a pressure chamber 3 l in volume, on 183 male white mice weighing 17 to 23 g. After a two hour fast, the animals were placed in the chamber, where the oxygen pressure was increased to 4.2—4.3 atm in 1—2 min. The carbon dioxide content in the chamber ranged from 0.3 to 0.5%. The first convulsive paroxysms under these conditions occurred in 6—18 min.

In a special series of control experiments, convulsions were induced by drugs--0.01% strychnine nitrate solution (0.01 ml/g of body weight) or a 1% metrazol solution (0.1 ml/g of weight).

In most of the experiments the entire body was stained. A 1% neutral red solution (Merck) was injected into the abdominal cavities of experimental and control animals, calculating 0.015 ml/g of body weight. At the end of the experiment all the mice were decapitated, and the brain, spinal cord, suprarenal glands, and gastrocnemius muscles were removed. The organs were placed first in Ringer's solution for 20 min and then in a 2% solution of sulfuric acid in 70% alcohol for the purpose of extracting the dye. After staining, the brain was divided into its hemispheres and lower portions. After 24 hrs the organs were taken out of the alcohol and dried to constant weight in an incubator at 37°. The colored alcohol was measure colorimetrically on an FEK-M photoelectric colorimeter.

The quantity of adsorbed dye was expressed in relative numbers according to the formula

$$E = \frac{\text{reading on the photometer scale}}{\text{weight of dried tissue (mg)}} \cdot 1000.$$

The figures obtained in the experiment were divided by the calculated figure for the control group derived by the same method, and the results were expressed in percentages.

In one series of experiments a study was made of intravital staining of isolated organs. The mice were decapitated immediately after being removed from the chamber. The brain was taken out first and placed in Ringer's solution for warm-blooded animals for 10 min. It was then transferred to a 0.1% solution of neutral red in Ringer's solution (without sodium bicarbonate) for 15 min at room temperature. After staining, the brain was washed in Ringer's solution, separated at the boundary between the cerebellum and olfactory lobes and placed in acidified alcohol in order to extract the dye. Study was also made of intravital staining of the spinal cord, suprarenal glands and muscles.

The numerical data obtained was analyzed statistically, and the root-mean-square error was calculated.

Results of the Experiments

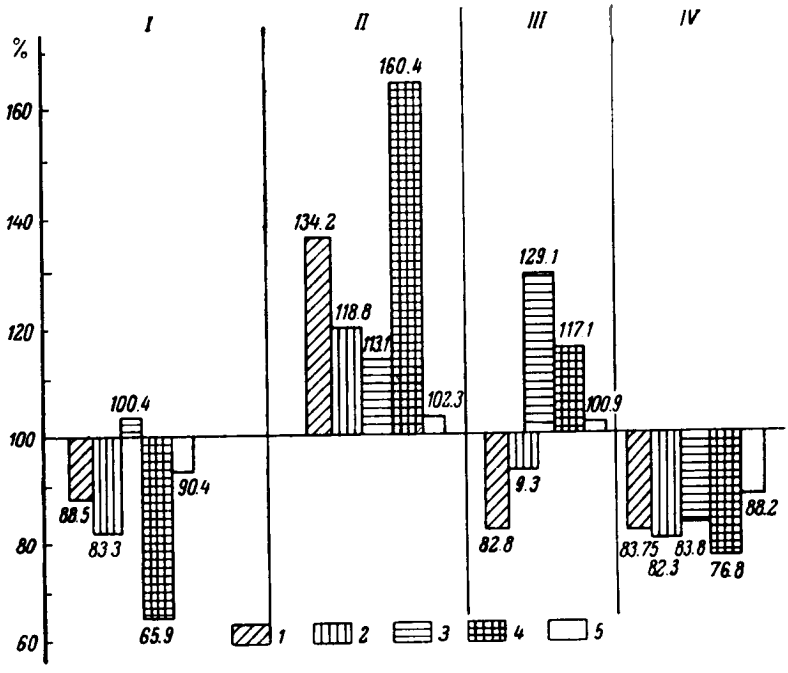
In the first 3—6 min after increase in the oxygen pressure to 4.2 atm, the mice moved about the chamber, sniffed its walls, washed and scratched themselves. Beginning with the 6th—15th min the animals became quieter, sat down, and walked about from time to time. Against this background the precursors of oxygen poisoning usually appeared (circus movements, tremor

of the head, slight twitchings of the limbs), after which a convulsive paroxysm occurred, first clonic and then tonic, lasting 5—15 sec.

At the end of the convulsive attack decompression was performed, which lasted about 3 min. The animals were under an oxygen pressure of 4.2 atm, a total of 14—35 min. After decompression coordination disorders were sometimes observed in the animals; however, painful stimulus applied to the hind paw resulted in reflex withrawal.

A pathological study of the organs in these animals revealed only very slight circulatory disorders, chiefly in the brain in the form of congestion and occasional light hemorrhages. Very similar changes are noted in the control animals after decapitation. In a number of mice there were small areas of atelectasis.

The results of the experiments using intravital staining are shown in the table and on the figure.



Adsorptive power of organs at various phases of the toxic effect of oxygen

on the abscissa, phase of the toxic effect of oxygen: I — preconvulsive; II — convulsive; III — immediately after reduction of oxygen pressure; IV — aftereffect phase. On the ordinate, the dye adsorption (in percent of the control). 1 — renal hemispheres; 2 — lower portions of the brain; 3 — spinal cord; 4 — suprarenal glands; 5 — muscle.

In the first series of experiments a study was made of the adsorptive power of the tissues under the toxic influence of oxygen in the preconvulsive period. For this purpose the mouse with dye injected into its abdominal cavity was placed in the chamber and kept under a pressure of 4.2 atm of oxygen until the precursors of oxygen poisoning appeared. It was determined that during this period adsorption of neutral red by the cerebral

Change in the binding of the dye at various phases of the toxic effect of oxygen

Series of experiments	Phases of the toxic effect of oxygen	Relative quantity of bound neutral red (in % of the control)				
		Cerebral hemispheres	Lower portions of the brain	Spinal cord	Suprarenal glands	Muscles
I	Preconvulsive	88,54 (−11,46±2,3)	83,3 (16,7 ± 3,4)	100,4 (+0,4±1,4)	65,9 (−34,1±5,5)	90,4 (−9,6±3,1)
II	Convulsive	134,2 (+34,2±2,7)	118,8 (+18,8±3,97)	113,1 (+13,1±6,2)	160,4 (+60,4±7,8)	102,3 (+2,3±2,5)
III	Postconvulsive	82,8 (−17,2±2,0)	93,0 (−7,0±2,2)	129,1 (+29,1±9,1)	117,1 (+17,1±4,6)	100,9 (+0,9±0,7)
IV	"	85,4 (−14,6±3,6)	—	—	—	102,1 (+2,1±1,2)
V	Aftereffect phase	83,75 (−16,25±3,7)	(−17,7±7,1)	83,8 (16,2±4,1)	76,8 (−23,2±6,2)	88,2 (−11,8±3,4)

Note. The first, second, third and fifth series represent staining of the intact organism; the fourth series, staining of isolated organs

hemispheres is reduced to 88.54% (−11.46±2.3); by the lower portions of the brain, to 83.6% (−16.7 ± 3.4), and by the suprarenal glands to 65.9% (−34.1 ± 5.5) (see the figure).

In the second series of experiments a study was made of the adsorptive power of organs of animals which had suffered convulsive paroxysms in the chamber at a pressure of 4.2 atm. The results revealed a distinct increase in the stainability of the cerebrum (134.2% or +34.2 ± 2.7%); the lower portions of the brain (118.8% or +18.8 ± 3.97%); the spinal cord (113.1 or +13.1 ± 6.2%) and particularly the suprarenal glands (160.4% or +60.4 ± 7.8%). The adsorptive power of muscles remained about the same (102.3% or +2.3± ± 2.5%).

In the third series of experiments a study was made of the stainability of organs in the postconvulsive phase. After the attacks of convulsions the mouse was removed from the chamber and given an intraperitoneal injection of the dye immediately after decompression or 60 min after. The staining was continued 20 min. The results of this series show a distinct reduction of the dye adsorption by the brain. The greatest reduction was noted in the cerebrum (82.8% or −17.2 ± 2.0%); a lesser reduction, in the lower portions of the brain (93% or −7 ± 2.2%). In the spinal cord, on the other hand, an increase was found in the adsorptive property (129.1% or +29.1 ± 9.1%). The suprarenal glands also bound the dye to a greater extent than the controls (117.1% or +17.1 ± 4.6%) (see the figure).

Sixty min after decompression, reduction of the adsorptive properties of the cerebrum was practically the same (83.75% or −16.25 ± 3.7%). The lower centers of the brain were characterized by a greater reduction of adsorptive properties (82.3% or −17.7 ± 7.1%); in the spinal cord and suprarenal glands increased adsorption was replaced by decreased adsorption (see the figure).

A study of the adsorptive power of the brain and muscles, also in the postconvulsive phase but with staining of the isolated organs, showed an appreciable reduction of the binding of neutral red by the cerebrum (85.4% or −14.6 ± 3.6%) (see the table).

Finally, in the last series 14 paired experiments were performed. Fifteen min after the injection of neutral red into the abdominal cavity a subcutaneous injection of 0.01% strychnine nitrate solution was given (0.01 ml/g of body weight). After 3—4 min, tonic convulsive attacks occurred. The experiments showed that the stainability of the cerebrum and lower centers of the brain did not change, whereas that of the spinal cord increased by 1 1/2 times (150.3% or +50.3 ± 14.9%). The opposite result was obtained in similar experiments, where the convulsions were produced by the injection of a 1% metrazol solution (0.1 ml/g of body weight). An increase in the stainability of the cerebral cortex (117% or +17 ± 3.9%) and subcortical nuclei (121% or +31 ± 4.3%) was found. The adsorptive properties of the spinal cord did not change.

Discussion of Results

In animals exposed to the effect of compressed oxygen a phasic change occurred in intravital stainability of the central nervous system and suprarenal glands.

The first (preconvulsive) phase (period of precursors of oxygen poisoning), is characterized by a reduction of stainability of the nervous tissue.

In the second (convulsive) phase, there is an increase in the binding of dye by the cerebrum.

Almost the same increase in adsorptive power was found by S. N. Romanov (1948), who studied the stainability of the cerebral cortex of rats during marked excitation in elaborating a conditioned defense reflex. It may be considered that increased ability to bind neutral red during the convulsive effect of oxygen is also explained by excitation of the cerebral cortex.

In the third (postconvulsive) phase a reduction is again observed in adsorptive power, which lasts an hour after convulsions cease.

Reduction of intravital stainability of the brains of mice after marked excitation resulting from electrical stimulation of the nerve has been described by S. N. Romanov. A similar biphasic change in stainability (reduction after an increase) has been observed by other authors (Zarakovskii and Levin, 1953; Golovina, 1958; and others).

Results of the intravital staining method suggest that during epileptiform convulsions produced by the toxic effect of oxygen the greatest excitation occurs in the cerebrum. Confirming this statement are experimental studies of intravital stainability of the central nervous system centers in convulsions induced by drugs with a well-known mechanism of action: strychnine, which chiefly affects the spinal cord, and metrazol, which acts on the inter- and midbrain. The experiments showed that stimulation of these portions of the central nervous system after injection of the corresponding doses of strychnine and metrazol was associated with a distinct increase in their adsorptive power.

The question may arise as to whether changes in adsorptive properties found after staining of the entire organism were a result of disorders of vascular permeability and hemodynamics. It is well known that oxygen has a vascoconstrictive effect. Therefore, during the period of convulsions a reduction might be expected in the supply of the dye to the organs, resulting in reduced stainability. The increased stainability of the brain attests to increase of the dye adsorption by nervous tissue. Experiments with intravital staining on isolated organs yielded the same results as experiments with the entire organism.

The method of intravital staining revealed that suprarenal glands undoubtedly participate in the pathogenesis of oxygen poisoning. Microscopic studies showed that neutral red chiefly stains the medullary substance of the suprarenal glands; staining of the cortical substance is barely noticeable. A marked increase in stainability of the medullary substance during the convulsive period may be considered an index of its great activity, which is maintained in the next period.

It is interesting that the changes in the adsorptive properties of muscles are so slight.

Conclusions

1. The method of intravital staining makes it possible to demonstrate early cytophysiological changes in various central nervous system centers and suprarenal glands under the toxic effect of oxygen.

2. A quantitative evaluation of these changes made it possible to determine the following phases of adsorptive properties of the nervous system centers: in the preconvulsive period the adsorptive power of the brain is reduced; during the convulsions such power increases considerably, and in the postconvulsive period a reduction re-occurs. Of all the nervous system centers, the cerebral cortex showed the greatest changes.

3. A study of the adsorptive properties of the suprarenal glands showed that the development of oxygen poisoning is accompanied by distinct changes in dye adsorption at various phases of the toxic effect of oxygen. This apparently indicates their considerable part in the pathogenesis of oxygen poisoning.

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G. L. Zal'tsman, I. D. Zinov'eva, S. D. Kumanichkin, and A. V. Turygina

EXPERIENCE IN THE COMPREHENSIVE STUDY OF THE CONDITION OF SOME SYSTEMS OF THE HUMAN BODY UNDER INCREASED OXYGEN PRESSURE

(Opyt kompleksnogo izucheniya sostoyaniya nekotorykh sistem organizma cheloveka v usloviyakh povyshennogo davleniya kisloroda)

Despite the large number of papers on the toxicity of increased oxygen pressures, its effect on many human body functions remains inadequately studied. Thus, no special investigation has been made of the human motor system under conditions of an increased oxygen pressure. A study of higher nervous activity by the conditioned-reflex method (Zhironkin, 1935; Rikkl' and Krivosheenko, 1948; Zilov, 1953) and by the electroencephalographic method (Lennox and Behnke, 1956; Gersch and Cohn, 1944; Stein, 1955; Alekseev, 1957; Chan—chun, 1960; and others) has been made only on animals.

The functions of the human cardiovascular and respiratory systems under conditions of increased oxygen pressure have been studied by many authors. It has been determined that initially a slowing of the pulse and respiration occurs; subsequently, in the toxic phase, an increase in their frequency and in blood pressure is observed. One of the early signs of the toxic effect of oxygen is constriction of the peripheral visual fields (Behnke, Forbes and Motley, 1936).

The aim of the present investigation was to study comprehensively the functions of a number of systems in man — central nervous system, motor, cardiovascular, and respiratory — under the initial toxic effect of oxygen.

Method

The studies were made on three subjects (divers, 21—23 years of age) in a dry compression chamber. The subjects breathed oxygen through a face mask in self-contained breathing apparatuses (the oxygen content was 90—93%). By supplying compressed air, the pressure in the chamber was raised to 3.5 atm in 2—3 min. This pressure was the safest and most convenient for studying the initial stages of oxygen poisoning.

The heart and respiratory rates were recorded on an MPO-2 oscillograph by means of skin electrodes* and a carbon-contact pickup. The blood pressure was recorded on an arterial oscillograph. The visual fields were determined on a portable perimeter.

* An EKP-5M electrocardiograph was used as an amplifier.

The muscle action currents were taken from the flexor digitorum communis of the right forearm, and recorded on an EMG- 4- OTM electromyograph. With the use of graded loads the record of action currents was made as follows: on an ergograph with a weight of 4 kg supported by index finger, and by compression of a hand dynamometer with forces of 8, 16, and 32 kg. The loads were changed at one- minute intervals.

The electroencephalogram was recorded on a subject sitting quietly with his eyes open. The cerebral action currents were tapped uniformly by means of skin electrodes from areas corresponding to the projections of the visual center and motor center of the right upper extremity. The action currents were amplified by means of special voltage amplifiers and recorded on an MPO- 2 oscillograph.

The higher nervous activity was studied by means of the following tests, listed according to the sequence of application: investigation of a previously elaborated motor reflex (pressure on a pedal in response to a lamplight) and delayed reflexes (pressure on a pedal in response to a red light, with a lag of 20 sec); determination of maximum discrimination of lights of different brightnesses; performance of a verbal experiment (5—10 stimulus words) with a subsequent check on memory; determination of the critical flicker frequency of a black and white disc or the critical frequency of stimuli on an FFS-O1 combination photic and audio stimulator. The assignment was given to draw a figure and write inscriptions for it; afterimages occurring after a three- second exposure to a luminous circle with a black diamond in the middle were determined.

The procedure for the investigation was the following: electroencephalographic tracing, a study of higher nervous activity, record of the indices of conditions of the cardiovascular and respiratory systems, and, finally, an electromyographic record. All the studies were initially made in a chamber under ordinary conditions, while breathing air, and then every half- hour while under pressure. The subjects were constantly observed during their time in the chamber. Each subject was exposed twice to the effect of increased oxygen pressure.

Results of the Investigations

Under conditions of increased oxygen pressure the subjects showed the following signs. During the first hour increased intestinal peristalsis was noted. After one hour and 32 min to one hour and 54 min the subjects complained of pains behind the sternum, labored respiration, headache, a black shroud before the eyes, and numbness of the fingers. At the same time, a dilatation of the pupils, facial pallor, and increased perspiration were observed. With increase in these phenomena the subjects were shifted to breathing air. Usually this occurred after being under pressure 1 hour and 55 min to 2 hours and 35 min.

Special studies of the conditions of certain body systems revealed the following. While breathing oxygen under pressure the subjects showed a gradual reduction in the frequency of cardiac contractions (by a maximum of 11—19 beats per min) with a simultaneous increase in blood pressure. No pronounced changes in the respiratory rate were noted. The peripheral visual fields did not change.

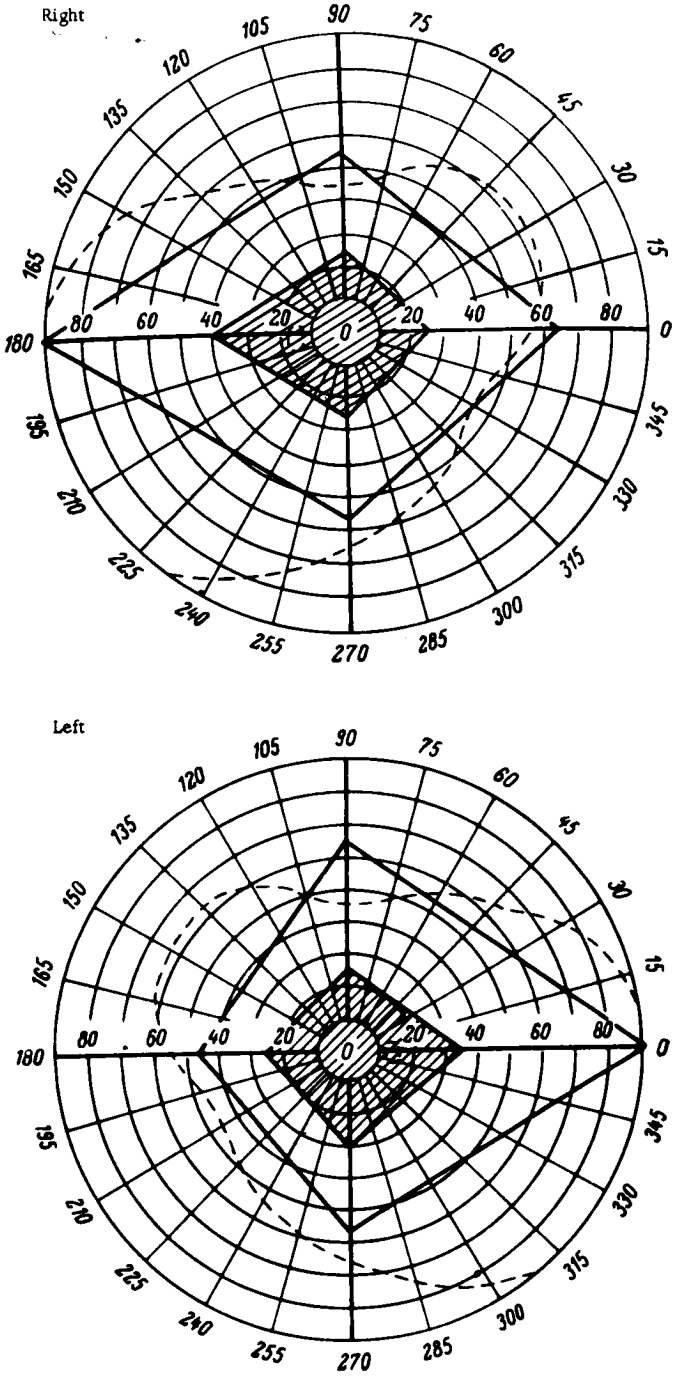


FIGURE 1. Constriction of peripheral visual field at the end of exposure to increased oxygen pressure (the visual fields were determined at 4 points)

At the end of the period of breathing oxygen, in three instances an increase in the heart rate was noted. In all subjects the blood pressure increased: the systolic, by 10—18 mm; the diastolic, by 21—25 mm. With the appearance of retrosternal pain, an increase in the respiratory rate by 4—10 per min was observed. In two cases a considerable concentric narrowing of the peripheral visual fields was observed (Figure 1).

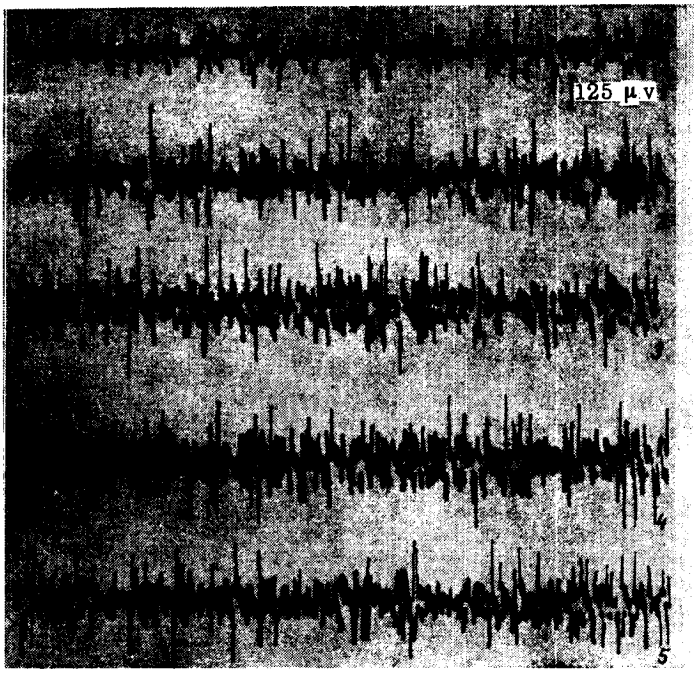


FIGURE 2. Change in action currents from the flexor communis digitorum of the right forearm on squeezing a dynamometer with a force of 32 g

1 — under normal pressure conditions while breathing air; 2 — after 10 min of being under increased oxygen pressure; 3 — after 40 min; 4 — after 2 hrs and 10 min; 5 — 35 min after switching over to breathing air. Time marking — 0,1 second intervals.

The EMG changes were noted as early as the first tracings — in the 10—30th min under pressure (Figure 2). The frequency and amplitude of the action potentials increased considerably over the initial figures. At the end of the time under pressure the frequency of the action potentials increased 41—108%; the amplitude, 75—180%. There was a direct relationship between the amplitude of the action potentials and the force applied. No changes were noted in the general EMG structure.

Changes in the electroencephalogram of the visual area were noted as early as the first tracings, 3 min after completion of compression (Figure 3, No. 2). The wave frequency increased to 45 per sec, and separate peaks appeared with amplitudes of 20—60 microvolts. At the end of the first hour an increase was observed in the amplitude of the waves,

and there were a large number of high-voltage peaks (40—180 microvolts) (Figure 3, No. 3). At the end of the second hour, reduction in the amplitude of the waves and multiple peaks were noted (Figure 3, No. 4).

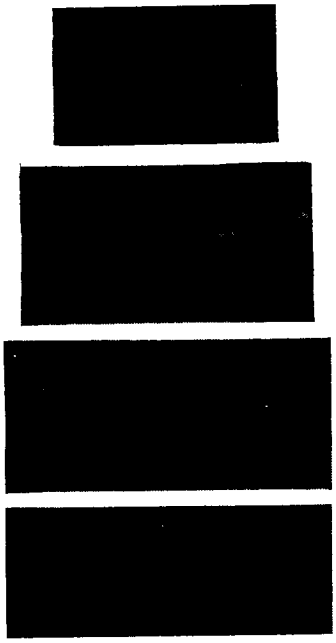


FIGURE 3. Action currents of the optic area

1 — under normal pressure conditions while breathing air; 2 — after 3 min of being under increased oxygen pressure; 3 — after 1 hr; 4 — after 2 hrs of being under increased oxygen pressure.

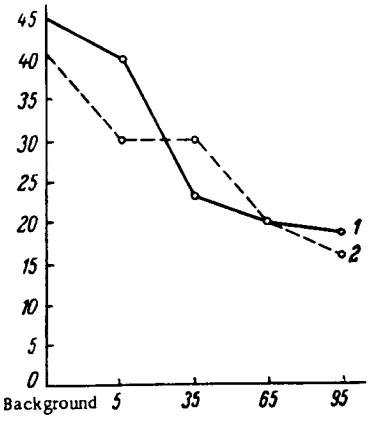


FIGURE 4. Frequency of fusion of photic and audio stimuli under an oxygen pressure of 2.5 atm

On the abscissa, frequency of the stimuli per sec; on the ordinate, time spent under pressure (in min). 1 — frequency of fusion of photic stimuli; 2 — frequency of fusion of audio stimuli.

Appreciable changes in the electroencephalogram of the motor center were recorded only after an hour under increased oxygen pressure. Low-voltage peaks and slow waves (10—12 per sec) appeared. After 1.5 hrs the number of peaks increased. Subsequently, this picture did not change appreciably.

Changes in higher nervous activity occurred as early as the first 5 and 10 min of breathing oxygen under pressure. A slight increase was noted in the latent period of motor and verbal reactions (by 8—14%), and there was a reduction in the motor and delayed reflexes (by 15—30%). After 2—2.5 hrs of being under pressure these changes decreased somewhat. The other tests and problems, including such complicated ones as tests of maximum discrimination, delayed reflexes, a verbal experiment with a check on memory, and drawing were carried out the same way under increased oxygen pressure as under normal pressure.

There was a considerable reduction of the critical frequency of photic and audio stimuli; changes in these indices proceeded in parallel. The maximum reduction toward the end of the time under pressure was 20—60% (Figure 4). After half an hour under pressure, pronounced changes also occurred in the latent period, color and shape of the after-images.

Discussion of Results

The clinical manifestations of the toxic effect of oxygen (facial pallor, numbness of the tips of the fingers, labored respiration, and others) occurring after 1 hour and 32 min to 1 hour and 54 min indicate disorders of the autonomic nervous system functions. Similar manifestations of the toxicity of oxygen have been described previously by many authors.

The reduced pulse and respiratory rates occurring under increased oxygen pressure against a background of very slight change in blood pressure may be interpreted as an adaptive reaction, in accordance with the ideas of other authors (Behnke et al., 1936; Haldane and Priestley, 1937; Zhironkin, 1955; Sorokin, 1960; and others). Subsequent increase in the respiratory and pulse rate, increase of blood pressure, and constriction of the peripheral visual fields indicate functional disorders of the cardiovascular and respiratory systems, which is also in agreement with the opinion of other authors (Behnke et al., 1956; Haldane and Priestley, 1937; Zhironkin, 1955; Sorokin, 1960; and others).

The ability to accurately perform the physical exercises assigned under increased oxygen pressure leads us to believe that no pronounced functional disorders of the motor system occurred in the subjects. However, the same exercises were performed with increased bioelectrical activity of the muscles. This suggests that efficiency is maintained under increased oxygen pressure in the presence of considerable stimulation of the motor system.

Changes in the electroencephalogram under conditions of increased oxygen pressure were similar to those observed in the preconvulsive state by many authors. The earlier and greater changes in the action currents of the optic area should be noted.

That the subjects could still carry out such complicated reactions as maximum discrimination of light intensity, delayed reflexes, and the verbal experiment under increased oxygen pressure leads us to believe that the complex cortical functions (analytical-synthetic activity, processes of internal inhibition, fine motor coordination, and others) do not change substantially. The slight changes in the latent periods of the verbal and motor reactions and in the magnitudes of the latter, as well as the considerable changes in the after-images and critical frequencies of photic and audio stimuli observed, may be explained by the change in the functional condition of the brain and possibly of the lability of the centers. The changes appear first in the sensory centers.

Comparing the results obtained by different methods of investigation, it should be noted that it was possible to demonstrate a number of latent changes in a subject as early as the first few minutes under increased oxygen pressure. The greatest changes occurred in the visual and, possibly,

auditory analyzers (change in the action currents of the optic area, reduction of the critical frequency of photic and audio stimuli, and change in the dynamics of after-images). However, despite these changes the complex behavioral reactions were retained. Therefore, it may be considered that changes demonstrated in the central nervous system are compensated for as are changes in the motor and cardiovascular systems.

Subsequently, with the appearance of pathological signs of oxygen poisoning (labored inspiration, retrosternal pain, black shroud before the eyes, facial pallor, abundant perspiration, and dilatation of the pupils) disorders were also noted in the cardiovascular and respiratory systems: increase in the heart and respiratory rates, increase in blood pressure, and constriction of peripheral visual fields. No new substantial changes occurred in the other systems studied.

Conclusions

1. The earliest changes occurring in the human body under the influence of high partial oxygen pressures and their subsequent dynamics can be demonstrated with simultaneous investigation of the physiological functions of a number of systems (central nervous system, motor, cardiovascular, respiratory).

2. In the initial period under increased oxygen pressure the functional changes recorded in the body systems were compensated for and did not appear as behavioral reactions.

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N. Ya. Sidorov

METHOD OF DETERMINING THE HEMODYNAMIC INDICES IN LONG- TERM EXPERIMENTS ON DOGS UNDER A HIGH PARTIAL PRESSURE OF OXYGEN (IN A PRESSURE CHAMBER)

(K metodike opredeleniya gemodinamicheskikh pokazatelei v khronicheskikh opytakh na sobakakh pri vysokom partsial'nom davlenii kisloroda (v barokamere))

One of the important indices in the effect of a high partial oxygen pressure on the body is the change in cardiovascular functions. This problem has been specially studied on human beings, chiefly at pressures no greater than 3 atm, during the initial period of the action of oxygen and until its convulsive effect began (Alveryd and Brody, 1940; Zhironkin, Panin, Sorokin, Farber, 1947; and others).

With animals, studies of the cardiovascular system may be made prior to and during the convulsive period. Until recently such studies were made only in short- term experiments. Blood pressure dynamics under these conditions have been studied on dogs by Bean and Rottschaffer (1937), P. M. Gramenitskii, P. A. Sorokin (1964), and others.

Clinically, for the purpose of judging the hemodynamic changes in the body, a number of indices are determined: blood pressure, arterial elasticity, pulse rate, stroke volume, peripheral resistance, and others (Savitskii, 1936, 1956; Kositskii, 1959; Arinchin, 1961; Wiggers, 1957).

In our investigations a study was made of the following indices: blood pressure (diastolic, lateral systolic), the rate of propagation of the pulse wave as an index of the tone in the large artery (Pravdich- Neminskii, 1950; Savitskii, 1956; Arinchin, 1961), the pulse (by the electrocardiogram) and the respiratory rates.

Method of Investigation

In working out the method we encountered considerable difficulties, which necessitated performing the experiments at a high barometric pressure.

The experiments were performed in a steel pressure chamber with a capacity of 100 l. Electric wires for recording the processes were introduced through the stuffing box of the chamber.

As with the other indices, the electrocardiogram from the electrocardiograph amplifier was recorded on an MPO- 2 oscillograph. The respiratory

and pulse waves of the carotid arterial wall were recorded by means of carbon-contact pickups, which were made of powdered carbon and nipple rubber*. For the purpose of increasing the sensitivity of the pickups, the latter were set up with permanent resistors in a bridge circuit (Sukachev, 1954).

Our tracings of the pulse waves of the carotid artery made it possible to determine the time of mechanical systole (from the beginning of the anacrotic wave to the incisura), the time of diastole, and the total period of the cardiac cycle (Figure 1). This data is necessary in calculating the stroke volume of the heart according to the Bremser-Ranke formula (1931). The record of pulse waves of the carotid artery was also used for determining the rate of propagation of the pulse wave by the V. V. Pravdich-Neminskii method (1950). This method makes possible simultaneous recordings of the electrocardiogram and pulse waves of the carotid artery in any one section.



FIGURE 1. Determination of the rate of propagation of the pulse wave by the Pravdich-Neminskii method

From top down: pulse waves of the carotid artery; time marking — 0,002 sec; ECG — second lead. Rate of movement of the tape — 250 mm/sec; the arrow indicates the incisura.

In dogs, blood pressure was measured in the carotid artery from an exteriorized skin flap by the tachooscillographic method of N. N. Savitskii during the period of cuff compression. We could not utilize the Savitskii mechanocardiograph, which provides for clinical recording of tachooscillograms (differential curves) because of its use of air transmission of arterial oscillations and of optical recording. It was impossible to use the arterial AO2-01 oscillograph, produced by the SKTB "Biofizpribor", because with increase in pressure and, accordingly, increase in the gas density, there is a change in the differentiating power of the differential AO2-01 piezoelectric manometer, by means of which a distance recording of the tachooscillogram may be made at normal barometric pressure.

Instead of the AO2-01 piezoelectric differential manometer we used a piezocrystal, which has differentiating properties in the area of mechanical frequencies from 0 to 50/sec, i.e., the EMF which occurs on its edges is a function of the change in frequency of the mechanical effect (signal) on the crystal (Turigin, 1959). Because the piezocrystal eliminates interference from the air gap of the cuff, connecting tubes, and differential manometer, its use considerably simplifies and renders more sensitive the differential recording system.

The capacity of the piezocrystal for transforming nonelectrical signals into electrical ones has been widely applied in medical practice (Langevin

* The resistance of the carbon-contact pick-up for recording the pulsations of the carotid artery was about 2,000 ohms; for recording respiration, about 1,200 ohms.

and Homez, 1933, 1934; Lepeshinskaya, 1943; Grinshtein, Bragina, and Goryd, 1954; Shvang, Fedorov, 1954; Marshak, 1956; Naumenko, 1957; Kositskii, 1959; Babskii, 1963; and others); however, we have found no indications in the available literature of the piezocrystal being used for recording the differential blood pressure curve in long-term experiments on animals under an increased barometric pressure.

The piezocrystal has a number of defects: fragility, increased hygroscopicity, and a sensitivity to temperature changes. However, if the piezocrystal is set in an airtight capsule made of Plexiglas (Figure 2) the influence of these defects on the accuracy of the measurement can easily be eliminated.

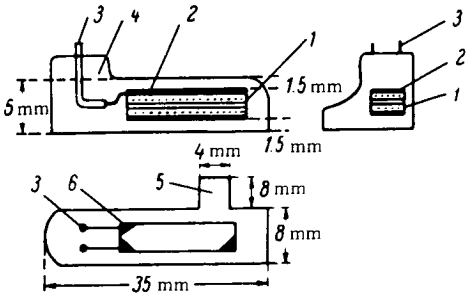


FIGURE 2. Diagram of the arrangement of an airtight Plexiglas capsule for the piezocrystal

1 — piezocrystal; 2 — rubber gasket 0.5 mm thick; 3 — outlet contacts from the piezocrystal; 4 — body of the capsule; 5 — projection of the capsule; 6 — points of attachment of the piezocrystal to the rubber gasket.

The signal from the piezocrystal is directed to the electrocardiograph amplifier or a UBP-01 amplifier made at the SKTB "Biofizpribor."

The frequency characteristic of the amplifier influences the shape of the differential curve. In working on the UBP-01 with a frequency filter (below 10 cycles/sec and above 1000 cycles/sec) the differential curve recorded is very similar to the tachooscillogram (Figure 3).

The differential curves recorded from the piezocrystal under normal and increased pressures are the same. Interpretation of the differential curve from the piezocrystal was made by the tachooscillographic method. The appearance of the first distinct negative wave in the lower portion of the differential curve corresponds to the minimum pressure; the appearance of the maximum oscillations, to the lateral systolic pressure. On the level of the lateral systolic pressure the positive waves decrease in amplitude (Savitskii, 1956).

For measuring blood pressure under pressure chamber conditions, a special system was worked out for compressing the carotid artery exteriorized in a skin flap so that the experimenter, who was outside the chamber, could make at will a blood pressure record (Figure 4). The principle of operation of the arterial compression system is that with the valve of the small tank open the gas, which is under a pressure of 150 atm,

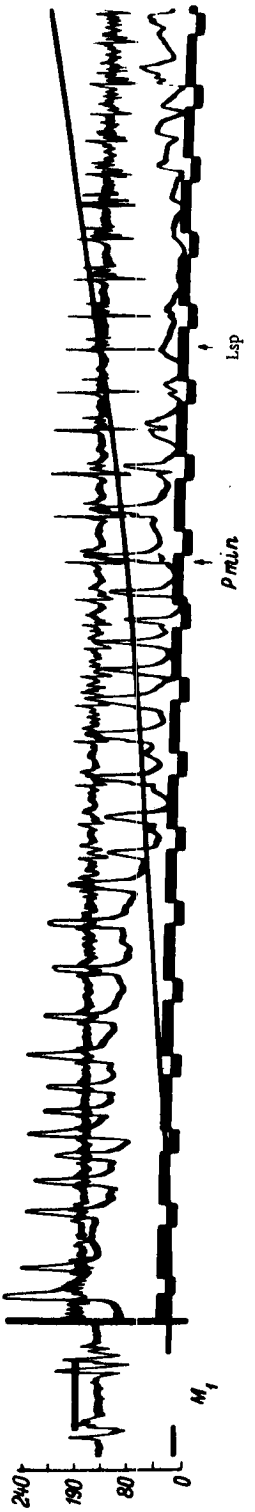


FIGURE 3. Determination of the pressure by Savitskii's tachooscillographic method and the Frank Wezler method during the period of compression of the cuff. From top down: differential curve recorded from piezocrystals; pulse waves of carotid artery; pressure in the cuff. Rate of movement of tape, 10 mm/sec. M_1 — imbalance of bridge before measurement of blood pressure; Lsp — lateral systolic pressure.

goes through a reducer to the cuff set on the vascular flap. If valve 2 is closed, there is an increase in pressure in the cuff when the gas enters, and the blood vessel is compressed. With valve 2 open decompression occurs, and the pressure in the cuff is reduced to the level of pressure in the chamber. During the experiment valve 2 is closed only during the measurement of the blood pressure.

For distance recording of the pressure change within the cuff, use was made of gauges set on the diaphragm of a Plexiglas capsule which was connected to the cuff through a T-piece (Figure 4). The signal from the strain gage was directed to a special amplifier (strain gage position) and then to the recorder. Within the limits of the pressures measured from 0 to 240 mm a linear relationship occurred between the value of the pressure in the cuff and the readings of the strain gages (Babskii, Gurfinkel', 1954; Liberman, 1958; Antonov, Vasilevskii, Naumenko, Sazonov, 1961; and others).

During the course of the work the strain gages were calibrated from time to time with a mercurial manometer. After the calibration a resistance of 50 kilohms was put into the circuit, which threw the bridge out of balance (M_1, Figure 3). This loss of balance in the bridge subsequently served as a standard control signal before each blood pressure measurement for determining the gain of the strain gage position. For the purpose of eliminating errors introduced by inconstancy of the gain, graphs were drawn showing the relationship between the output signal when calibrated as a function of the gain. With consideration of this relationship, the true blood pressure value was determined.

The minimum pressure, aside from recording by the tachooscillographic method, was measured by a carbon-contact pick-up with the use of

the Frank Wezler method (1931). These authors suggested determining the minimum pressure at the time of occurrence of the negative wave before the anacrotic wave of the sphygmogram or the pointed peak on the anacrotic wave, the "preanacrotic" phenomenon. Their data has been confirmed by the works of other authors (Bauereisen, Paerisch, Schmerso, 1953; Drube and Anschütz, 1954; Wiggers, 1957). Independently of Frank and Wezler, the "preanacrotic" phenomenon has been observed by other investigators (Erlanger and Hocker, 1916; Bramwell and Hickson, 1926).

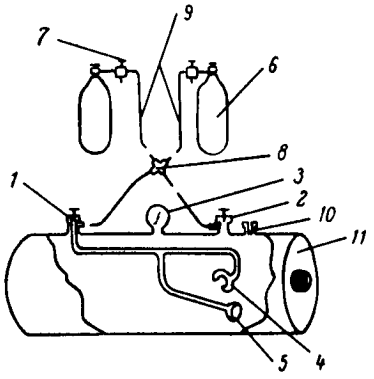


FIGURE 4. Diagram of system for compressing carotid artery

1, 2 — valves of the chambers; 3 — chamber manometer; 4 — cuff; 5 — Plexiglas capsule; 6 — 1,3-liter tanks (operating pressure, 150 atm); 7 — reducer (oxygen-supply mechanism); 8 — cross-connection; 9 — air ducts; 10 — stuffing box for electric wires; 11 — chamber.

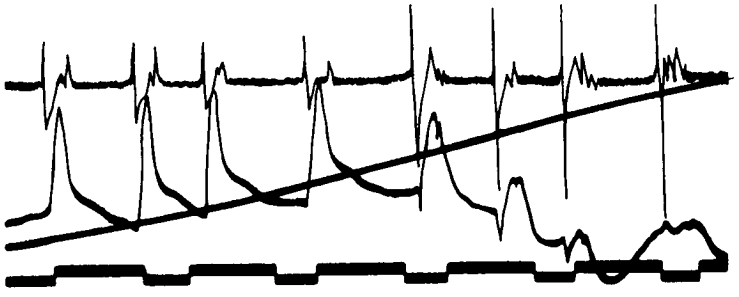


FIGURE 5. Determination of the diastolic pressure by the Savitskii tachooscillographic method and the Frank-Wezler method

From top down: differential curve from the piezocrystal; pulse waves of the carotid arterial wall; pressure in the cuff. Time marking — 1-second intervals. Rate of movement of the tape, 10 mm/sec.

As is evident from Figure 5, the appearance of a negative wave on the differential curve during the period of compression corresponds to the occurrence of a "preanacrotic" phenomenon on the sphygmogram. *

General Procedure for Performing the Experiments and Their Results

Before putting the animal into the chamber, skin electrodes were placed on it for recording the electrocardiograms in the second lead. A cuff was set on the vascular flap, and under it a capsule containing a piezocrystal was placed so that the tip of the capsule projection was located over the pulsating blood vessel. A carbon-contact pick-up was located distal to the cuff.

After the application of the pick-ups a record was made of the initial temperature in the chamber in which the dog was placed. After 18—20 min we began to record the initial background of the animal in the chamber with the cover open (25 min). After this, the cover of the chamber was closed, and the chamber was ventilated with oxygen for 2—3 min or, depending on the purpose of the experiment, with air. Compression was then carried out at a rate of 1 atm/min. The diastolic pressure did not exceed 3—4 absolute atm. The chamber was ventilated with oxygen for 1 minute every 20 min. The animal remained under pressure until oxygen-induced convulsions appeared, after which decompression was performed. During the period of decompression a gas sample taken from the chamber was analyzed for carbon dioxide and oxygen. The record of the indices was made every 5 min during the course of the experiment.

Conclusions

1. With the aim of studying hemodynamic changes in long-term experiments on dogs the following methods were modified to apply to working conditions under increased pressure: the tachooscillographic method of N. N. Savitskii, the Frank-Wezler method for measuring the blood pressure, and the V. V. Pravdich-Neminskii method for determining the rate of propagation of the pulse wave in large arteries.

The Savitskii method required the most improvements: the main unit of the mechanocardiograph — the differential manometer — was replaced by a piezocrystal, which simplified the method and increased the accuracy of the differential curve recording. The optical system of the mechanocardiograph was replaced by a UBP-01 amplifier and MPO-2 oscillograph.

For recording the diastolic pressure by the Frank-Wezler method under conditions of increased pressure, a highly sensitive air capsule with optical recording was replaced with a carbon-contact pick-up set in a bridge circuit. This carbon-contact pick-up was used for recording the rate of propagation of the pulse wave.

* In Figure 3 a tracing is given in which the appearance of the negative wave in the differential curve corresponds to the recording of the last pulse curve of ordinary configuration. Such a possibility has been mentioned by Wiggers (1957). According to our tracings the variant described by Wiggers is rarely encountered.

2. The method worked out makes it possible to determine directly the dynamics of the following hemodynamic indices: diastolic and lateral systolic pressures, rate of propagation of the pulse wave as an index of tone of the great vessels and the rhythm of cardiac contractions.

On the basis of the data obtained the derivatives of the following hemodynamic indices may be calculated: stroke volume, minute volume, and peripheral resistance.

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A. F. Panin

THE BLOOD AND SPINAL FLUID SUGAR, LACTIC ACID, AND INORGANIC PHOSPHORUS IN DOGS WITH HYPEROXEMIC AND HYPOXEMIC CONVULSIONS

(Soderzhanie sakhara, molochnoi kisloty i neorganicheskogo fosfora v krovi i spinnomozgovoi zhidkosti u sobak pri gipero-i gipoksemicheskikh sudorogakh)

Under certain conditions both hyperoxemia and hypoxemia may cause death, usually preceded by convulsions.

Publications of M. P. Brestkin's laboratory show that hyperoxemic and hypoxemic convulsions are associated with serious physiological disorders in a number of body organs and systems (Zhironkin, 1940, 1956; Zagryadskii, 1954; Gramenitskii, Sulimo-Samuillo and Tripolov, 1955; Voino-Yasenetskii, 1958; and others), and that there are a number of common mechanisms causing the convulsive seizures induced by reduced and increased oxygen pressures; specifically, both types of convulsions have a reflex origin.

In the literature available to us we have not found any thorough investigations on the comparative evaluation of the biochemical indices of the blood and spinal fluid in dogs during hyperoxemic and hypoxemic convulsions.

We therefore decided to study the nature of metabolic processes in hyperoxemic and hypoxemic convulsions, and to compare this data with physiological investigations by the authors mentioned.

Experiments and Methods of Investigation

The experiments were performed on six dogs, three of which were studied for the effect of increased oxygen pressures, and three for reduced pressures. In this way, we avoided superimposing one effect upon the other.

The convulsions were studied in increased and reduced atmospheric pressure chambers.

The hyperoxemic convulsions occurred at an oxygen pressure of 3—4 atm; the hypoxemic convulsions, at altitudes from 10,000 to 15,000 m, which correspond to pressures of 90—198 mm Hg.

To avoid the effect of sharp pressure drops which cause serious disorders in a number of organs (gastrointestinal tract and other cavities) the animals were raised and lowered in two stages: in the case of study

of hyperoxemic convulsions the dogs were first under a pressure of 2.5 atm; in the study of hypoxemic convulsions they were raised to an altitude of 8,000 m. The preliminary hypoxemic and hyperoxemic states were always created for one hour, after which the animals were slowly raised or lowered to the height or depth mentioned above until clearly expressed signs of a convulsive state appeared.

Fasting dogs were always used in the experiment. In the control and main experiments, the blood was taken from the cervical vein, and spinal fluid from the suboccipital space. In the main experiments blood and spinal fluid were always taken 2—3 min after the animals had been removed from the chamber, while they were still in a convulsive state.

In the blood and spinal fluid a study was made of the following constituents: sugar (by the Hagedorn-Jensen method), lactic acid (by the Friedman, Cotonio, and Schaeffer method) and inorganic phosphorus (by the Fiske-Subbarow method). During the experiments the general behavior of the animals was observed: the times of occurrence of dyspnea, coordination disorders, convulsions, etc., were noted.

Results of the Investigation

The results of analyses of the blood and spinal fluid in dogs with hyperoxemic and hypoxemic convulsions are shown in Tables 1 and 2.

TABLE 1

The effect of hyperoxemic convulsions on the sugar, lactic acid, and inorganic phosphorus contents of the blood and spinal fluid of three dogs (average data of 12 experiments)

Dog	Time of taking blood and spinal fluid	Blood			Spinal fluid		
		Sugar (in mg)	Lactic acid (in %)	Phosphorus (in mg)	Sugar (in mg)	Lactic acid (in %)	Phosphorus (in mg)
Ugol'	Before convulsions	100	18	2.8	70	14.6	1.4
	During convulsions	188	165.2	6.4	100	30.2	1.1
Volchok	Before convulsions	74	9.4	4.6	74	15.4	1.8
	During convulsions	172	157.9	8.7	90	36.9	2.7
Chernysh	Before convulsions	97	13.4	2.9	68	13.8	1.4
	During convulsions	196	93.3	9.5	143	28.4	2.1

From the tables it is evident that all the blood and spinal fluid indices which we studied in dogs during hyperoxemic and hypoxemic convulsions underwent distinct changes.

The sugar of the blood and spinal fluid in dogs with hyperoxemic convulsions was markedly elevated. It increased 90—150% in the blood and 80—120% in the spinal fluid. In hypoxemic convulsions the increase in sugar was noted only in the blood, and was smaller (by 10—50%); in the spinal fluid its content remained unchanged or even decreased somewhat.

TABLE 2

The effect of hypoxemic convulsions on the sugar, lactic acid, and inorganic phosphorus contents of the blood and spinal fluid of three dogs (average data of 12 experiments)

Dog	Time of taking blood and spinal fluid	Blood			Spinal fluid		
		Sugar (in mg)	Lactic acid (in %)	Phosphorus (in mg)	Sugar (in mg)	Lactic acid (in %)	Phosphorus (in mg)
Druzhok	Before convulsions	96	11.7	3.9	72	15.8	1.6
	During convulsions	187	99.9	1.4	23	59.4	0.9
Volk	Before convulsions	78	9.6	4.6	68	18.0	1.8
	During convulsions	163	67.6	3.1	50	58.0	1.8
Zhuchok	Before convulsions	81	13.6	4.1	70	16.7	1.7
	During convulsions	149	48.4	3.1	61	50.1	1.4

It was then determined that the quantity of lactic acid in the blood during hyperoxemic convulsions also increased considerably; sometimes this increase was 1,000—1,500%. In the spinal fluid the lactic acid also increased but to a lesser degree (100 — 300%). In hypoxemic convulsions an increase is also noted in the blood lactic acid by 800—1,000%; in the spinal fluid the increase is approximately the same as in hyperoxemic convulsions.

Finally, the quantity of inorganic phosphorus in the plasma and spinal fluid in hyperoxemic convulsions was found to increase distinctly; on the average, the phosphate content increased two to three times in plasma and 1,5—2 times in spinal fluid. In hypoxemic convulsions the content of inorganic phosphorus in the plasma and spinal fluid remained unchanged or even decreased somewhat. Apparently, this difference in the phosphate content of the blood may be explained by the characteristics of the acid-base balance during these opposite effects.

From a comparison of the results of observations of the behavior of animals under increased and reduced oxygen pressures it is evident that the nature of the body's reaction to these opposite effects has many features in common, on the one hand and, on the other, shows great differences.

Of the general signs characterizing the hyperoxemic and hypoxemic convulsions mention should be made of the following: 1) rigidity of the cervical muscles; 2) salivation; 3) coordination disorders; 4) involuntary urination and defecation; 5) the appearance initially of local spasms (muscles of the head, neck and limbs) and then of generalized convulsions; 6) a respiratory disorder, and in both cases fast superficial respiration occurs before and during the convulsions.

The difference in the body's reactions to increased and reduced oxygen pressure is expressed in the following characteristics.

Firstly, the duration of the convulsive seizures after the discontinuance of the effect of the gas medium varies. In hyperoxemia, as a rule, they

last longer; sometimes, the oxygen-induced convulsions go on for several hours. Hypoxemic convulsions stop 5—6 min after the effect of the altered gas medium has been removed.

Secondly, an essential difference is noted in the conditions of the animals which have suffered from hyperoxemic and hypoxemic convulsions. When the animals which had suffered hypoxemic convulsions are brought down from altitude they recuperate and following the convulsions they eagerly take food. In the case of hyperoxemic convulsions, on the other hand, a number of serious sequelae usually remain. The coordination disorder was observed in these animals for a long time (sometimes more than a day); frequently the animals were indifferent to their surroundings and, finally, dogs which had had hyperoxemic convulsions did not eat for a long time.

Thirdly, there is an essential difference between the degrees of expression of the actual convulsions. Hypoxemic convulsions usually are mild; movements of the muscles of the extremities and of other parts of the body usually are localized. In the case of oxygen-induced convulsions, on the other hand, the strength of muscular contraction is great.

Fourthly, an essential difference is noted in respiratory rhythm in the preconvulsive state: in hypoxemia the rhythm of the respiratory movements is considerably increased; in hyperoxemia, conversely, it is reduced.

Fifthly, rigor mortis sets in very quickly in a dog which has died of hyperoxemic convulsions; in hypoxemic convulsions, on the other hand, the muscles remain soft for a long time.

Discussion of Results

When the metabolic findings and the characteristics of the convulsions in dogs with hypoxemia and hyperoxemia are compared, the following generalizations may be made.

Our data shows that hyperoxemic and hypoxemic convulsions in dogs are accompanied by a marked increase in the lactic acid of the blood and spinal fluid. This indicates the development of a considerable oxygen debt in both cases. In hypoxemic convulsions, this is caused by reduced oxygen tension in the body tissues because of the marked reduction of the partial oxygen pressure in the inhaled air. In hyperoxemic convulsions the oxygen debt develops, conversely, under conditions of an abundance of oxygen in the body tissues, which results in the depression of activity of enzyme systems providing for oxidation-reduction processes. This is also evidenced by the studies of A. F. Panin (1953, 1960), L. I. Grachev (1954), Z. S. Gershenovich and A. A. Krichevskaya (1960), and others, who showed that increased oxygen pressure leads to a distinct reduction of protein, carbohydrates and gas metabolism as well as to an inhibition of oxidation-reduction reactions and the synthetic activity of cerebral, muscular, hepatic and other tissues.

Therefore, the investigations of the above authors and our own data on the lactic acid content of the blood and spinal fluid give us the basis for the belief that increased oxygen pressure causes serious disorders in the utilization of oxygen by the body tissues.

In addition, there is an essential difference between the values of these metabolic indices in hyperoxemic and hypoxemic convulsions: their level was considerably greater during the breathing of oxygen under increased pressure. We explain this difference by the strength of the excitatory process of the central nervous system, the duration of convulsive seizures, and, finally, by the strength of the muscle contractions. However, we do not yet know the details of the mechanism of the central nervous system disorder during these opposite effects. These problems should be solved, as they are undoubtedly important both theoretically and practically.

Summing up the above material, we consider it possible to conclude that underlying the effect of increased and reduced oxygen pressure under certain conditions are general mechanisms of a disorder of central nervous system activity. The hyperoxemic and hypoxemic convulsions are characterized by a considerable increase in the blood lactic acid content; in the former case this increase is brought about by interference with tissue oxygen utilization; in the latter, by reduction of the oxygen tension in the tissues.

Conclusions

1. There are a number of features in common in the development of hyperoxemic and hypoxemic convulsions in animals and simultaneously there are essential differences.
2. Hyperoxemic and hypoxemic convulsions cause a considerable increase in the blood lactic acid content of dogs. In the former case the increase is caused by an interference with the oxygen utilization by the tissues; in the latter case, by a reduction of the oxygen tension in the tissues.
3. The blood sugar content of dogs with hyperoxemic and hypoxemic convulsions is markedly increased.
4. The blood inorganic phosphorus in dogs with hyperoxemic convulsions is distinctly elevated; in hypoxemic convulsions, the phosphorus level remains unchanged or is somewhat reduced.

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V. N. Zvorykin

THE TYPOLOGY OF HIGHER NERVOUS ACTIVITY CHARACTERISTICS IN DOGS UNDER BAROMETRIC PRESSURE CHANGES

(Tipologicheskie osobennosti vysshei nervnoi deyatel'nosti sobak pri izmenenii barometricheskogo davleniya)

The differences in the behavior and mental activity of individuals under conditions of reduced air pressure in mountain climbing, airplane flights or pressure-chamber tests were noted long ago by many investigators. In studying changes in the physiological functions during anoxia in animal experiments, physiologists also noted different variants of behavioral reactions in animals of the same species. However, the physiological mechanisms of these differences in behavior and mental activity continue to be unclear, partly because little use has been made of I. P. Pavlov's teaching of the typology of higher nervous activity (Pavlov, 1927, 1928, 1935), and because the nature of high-altitude reactions has not been compared with an objective characterization of the basic properties of the nervous processes in the cerebral cortex — strength, equilibrium, and mobility of excitation and inhibition — or with the functional limit of cortical cells.

On this basis we decided to study the effect of rarified air and anoxia on higher nervous activity (Zvorykin, 1951, 1953), and to determine the characteristics of these changes in dogs with different types of nervous activity.

Method

The investigation was made on dogs by the method of conditioned salivary reflexes to food with the use of stereotype of positive conditioned stimuli and differentiation. Of the nine dogs prepared for the experiments, four differed greatly in their higher nervous activity types, which were determined by a somewhat modified "low standard" method. In addition to obtaining data from the elaboration of conditioned reflexes, tests were performed involving starvation, caffeine, bromine, the effect of a very powerful stimulus, extension of the positive conditioned reflex, prolongation of the action of the differentiating stimulus, change in the biological significances of the positive and inhibitory conditioned stimuli, and a check on the dynamic stereotype with an "indicator" stimulus.

The experiments were performed in a pressure chamber with rarefaction of the air, corresponding to altitudes from 1,000—8,000 m above sea level.

Experimental Data

A test of the nervous system type showed that in the dog Bars the excitatory and inhibitory processes of the cerebral cortex were strong, balanced, and mobile (I. P. Pavlov's lively type). The nervous processes in the cerebral cortex of the dog Ryzhii were not so strong as in Bars, and were inert, particularly with respect to inhibition (the weak variant of the quiet type, according to I. P. Pavlov). In the dog Belyi a marked predominance of a strong excitatory process over weak inhibition was demonstrated in the cerebral cortex, and it was therefore designated as the strong, balanced type (unrestrained, according to I. P. Pavlov). The higher nervous activity type of the dog Bembi could be characterized as a weak variant of the unbalanced type (with a predominance of the excitatory over the inhibitory process).

Along with general changes in higher nervous activity in the experimental dogs during rarefaction of the air and anoxia which we have described previously (Zvorykin, 1951, 1953), some essential characteristics and differences between the reactions of the individual dogs were also demonstrated.

TABLE 1

Conditioned reflexes (salivation in drops for 20 sec) in dogs at normal atmospheric pressure (numerator) and at an altitude of 6,000 m (denominator)

Conditioned stimulus*	Bars	Belyi	Ryzhii	Bembi
Bell	9/7	11/10	8/0	6/0
Light	5/0	8/6	5/1	2/0
M_{120}	8/5	9/2	6/1	4/0
M_{60}	1/4	4/5	0/1	1/0
Bell	8/5	12/7	7/0	3/0
Light	4/3	6/5	4/0	2/0
M_{120}	6/3	8/5	5/0	2/6
Total for the experiment	41/27	58/40	35/3	20/6

* M_{120} and M_{60} represent metronomes operating at 120 and 60 beats/min.

Thus, it was found first of all that the stage of excitation characteristic of the action of low altitudes and of the initial period of anoxia, was different in degree and frequency in different dogs. It was observed frequently, was distinct, and accompanied by increased motor activity in the dogs Bars and Belyi and was expressed extremely rarely and slightly in the dogs Ryzhii and Bembi. In these latter annoxia always began with the inhibitory stage, usually characteristic of the later period of anoxia and of high altitudes. In the dogs Ryzhii and Bembi inhibition of conditioned reflexes and adynamia were observed even at low altitudes (1,000—4,000 m), whereas in the dogs Bars and Belyi inhibition developed

only at altitudes of 7,000—8,000 m. The degree of inhibition of the positive conditioned reflexes in the dogs was also different. Reduction of the magnitudes of the conditioned reflexes and prolongation of the latent period were least in the dogs Bars and Belyi and greatest in the dogs Ryzhii and Bembi (see Table 1).

Considerable differences were also found in the effect of rarefaction of the air in the chamber on conditioned inhibition. Thus, in the dogs Bars and Ryzhii disinhibition of differentiation at altitude was rarely observed; sometimes, differentiation even became greater, while extinction of the conditioned reflexes occurred more quickly because of lack of reinforcement than at normal atmospheric pressure. In the dogs Bembi and Belyi disinhibition occurred very often, not only during the stage of excitation but also in the inhibitory stage. A deepening of differentiation at an altitude in the dog Ryzhii very often gave rise to prolonged after-inhibition, which sometimes lasted more than 15—20 min. In Bembi the after-inhibition developed less often; in the dogs Bars and Belyi it was not seen.

Phasic states (hypnotic phases) in the cerebral cortex, which represent one of the characteristic changes in higher nervous activity at altitudes, were also expressed differently in different dogs. In the dog Ryzhii anesthetic and inhibitory phases occurred most often; in Belyi, most common were an equalizing phase on a high level and an ultraparadoxical phase; in Bembi, all the phasic states occurred equally often, even at low altitudes (1,000—4,000 m). They occurred least often in the dog Bars. It is interesting that in Belyi the equalizing phase occurred with a high level of conditioned reflexes, which was evidence of an increase in excitability of the cerebral cortex; in the dogs Bembi and Ryzhii it always occurred at a low level, evidencing development of inhibition (Table 2).

TABLE 2

Equalizing phase in the function of the cerebral cortex in the dogs Belyi and Bembi under normal atmospheric pressure (numerator) and with rarefaction of the air (denominator)

Conditioned stimulus	Conditioned salivary reflex (drops in 20 sec)	
	Belyi	Bembi
Bell	9/9	4/3
Light	2/9	2/3
M_{120}	9/9	7/4
M_{60}	3/0	5/0
Bell	8/5	5/2
Light	7/0	3/2
M_{120}	4/11	4/3

The dynamic stereotype changed in different ways at altitude (Table 3).

TABLE 3

Check on the dynamic stereotype of dogs Bembi and Belyi at normal atmospheric pressure and at an altitude of 4,000 m

Indicator stimulus	Conditioned salivary reflex (drops in 20 sec)			
	Bembi		Belyi	
	Normal atmospheric pressure	Altitude 4,000 m	Normal atmospheric pressure	Altitude 4,000 m
Light instead of bell	4	3	8	5
Light	0	4	5	4
Light instead of M_{120}	4	2	4	8
Light instead of M_{60}	2	1	6	5
Light instead of bell	—	—	6	6
Light	—	—	9	3
Light instead of M_{120}	—	—	3	8

Thus, in the dog Bembi under normal atmospheric pressure conditions the dynamic stereotype was distinct. At altitude the dynamic stereotype, which could be checked by the subsequent use of a weak stimulus, changed in the manner of the equalizing and paradoxical phases. The conditioned-reflex reaction to a light stimulus, applied at the place where the bell or M_{120} was usually administered, was found to have an equal or decreased effect than when used in its own place. In the dog Belyi at normal atmospheric pressure it was practically impossible to detect the formation of a dynamic stereotype. When the system of stimuli was replaced by one stimulus used after a lag, the conditioned reflexes to its effect were modified in a most unexpected way. At altitude this dog showed a distinct dynamic stereotype.

TABLE 4

Adaptation of dogs during repeated ascents in a pressure chamber

Name of dog	Magnitude of conditioned salivary reflex during the experiment performed at normal pressure (average for 10 days)	Conditioned salivary reflex during the experiment performed at an altitude of 6,000 m					
		First ascent	Second ascent	Third ascent	Fourth ascent	Fifth ascent	Sixth ascent
Bars	41.7	27	18	21	54	37	44
Ryzhii	36.2	3	13	16	26	39	42

Recovery of the conditioned reflexes occurred differently after descent. They were regained soonest and most completely in the dog Bars: recovery began even during the descent, and the conditioned reflexes sometimes returned to normal as soon as normal atmospheric pressure was restored to the chamber. The conditioned reflexes of the dog Belyi were regained somewhat more slowly than in the dog Bars. Only differentiation remained disinhibited, usually for a long time after descent. In the dog Ryzhii the recovery of the positive conditioned reflexes occurred very slowly, and sometimes it was impossible to reproduce them during the experiment. Differentiation continued to be absolute. Frequently, the conditioned reflexes in Bembi could not be brought back for several days.

The effect of the differential stimulus sometimes caused a marked deterioration in the conditions of the dogs Belyi and Bembi under considerable rarefaction of the air. There was an increase in dyspnea, and motor defence reactions were expressed; in two experiments clonic convulsions, opisthotonos and respiratory arrest occurred in the dog Bembi immediately after the action of M_{60} at altitudes of 7,000 and 8,000 m.

It was very important to check how high- altitude adaptation occurs in dogs with different types of nervous activity. For this the dogs Bars and Ryzhii were elevated to altitudes of 6,000 m daily for 6 days. The experiments showed that by the 5th—6th day the changes in their conditioned reflexes became minimal, and were practically the same in magnitude as at normal atmospheric pressure (Table 4).

Discussion of Experimental Data

The data presented shows that there is a definite relationship between the nature and degree of changes in higher nervous activity in dogs under rarefaction of the air, on the one hand, and the basic characteristics of their nervous processes, on the other. Higher nervous activity changes were least in the dog with the highest functional limit of the cerebral cortex (Bars) and greatest in the dog with the lowest functional limit (Bembi). Of the two other dogs changes in higher activity were less in the one in which the functional limit of cortical cells was greater (Belyi).

The phase of excitation with rarefaction of the air is observed chiefly in animals with quite a strong excitatory process (Bars and Belyi). The early and profound depression of the conditioned reflexes and the lesser degree of expression of the excitatory phase in dogs with an insufficiently strong inhibitory process (Ryzhii and Bembi) is evidently caused by early development of inhibition, even with slight degrees of rarefaction of the air.

The nature of the higher nervous activity changes in dogs with rarefaction of the air also depends on the strength of the inhibitory process in the cerebral cortex. Proof of this is that with rarefaction of the air the reaction to the differential stimulus does not change in dogs with strong inhibition and absolute differentiation (Bars and Ryzhii), whereas dogs with a weak inhibitory process (Belyi and Bembi) show early disinhibition of differentiation.

The mobility of the nervous processes in the cerebral cortex plays a great part in the reaction of dogs to the effect of rarefied air. Good mobility of the nervous processes (Bars) remains practically unchanged with rarefaction of the air. If the mobility of both nervous processes was slight or

if one was inert, this inertness was made even greater with rarefaction of the air. As a result, a very prolonged after-inhibition of positive reflexes was observed after the use of differentiation at altitude in the dog Ryzhii, whose inhibition was characteristically inert. In the dog Belyi, with rarefaction of the air there was even a greater increase in the characteristic inertness of its excitatory process, which gave rise to disinhibition of differentiation after the use of positive conditioned stimuli.

Changes in the dynamic stereotype also depended on the type of nervous system. It was impaired in the same manner as in hypnotic phases in dogs with insufficiently strong excitatory or inhibitory processes and did not change in the dog Bars. In the dog Belyi, reduced mobility of the nervous processes under the influence of rarefied air facilitated retention of the dynamic stereotype, because traces of excitation or inhibition evidently were maintained for a longer time and in a more stable form than usual in the cerebral cortex under these conditions.

The experiments showed that different frequencies and different natures of phasic states in the function of the cerebral cortex in both dogs also depend on the strength, equilibrium and mobility of the nervous processes and the functional limits of cerebral cortical cells with rarefaction of the air. In the dog with the highest functional limit (Bars) phasic states were observed least often; in the animal with the lowest functional limit (Bembi) they were observed most often and even at low altitudes. The early appearance of the inhibitory phase was observed in dogs with a lower cerebral cortical functional limit (Bembi). The ultraparadoxical phase was manifested only in the dog with the weakest inhibitory process (Belyi), which evidently facilitated positive induction from areas of the cerebral cortex which had gone into a state of transmarginal inhibition. The anesthetic phase was observed most often in the dog Ryzhii whose conditioned reflex to a weak stimulus (light) had been elaborated for a long time and with difficulty. This reflex was also the first and most deeply inhibited under the influence of rarefied air.

The rate and nature of recovery of conditioned reflexes after the descent also depend on the type of nervous activity. The experiments showed that with strong, balanced and mobile nerve processes and a high cerebral cortical functional limit (Bars) the conditioned reflexes are regained most completely and most quickly; they are recovered least completely and most slowly in dogs with a lower cerebral cortical functional limit (Bembi, Ryzhii).

The experimental data on the influence of the inhibitory stimulus on the nature of high-altitude reactions of the dogs Belyi and Bembi suggest that the conditioned stimuli acting on the animals with rarefaction of the air, can, under certain conditions, also affect their resistance to altitudes. Thereby, the effect of inhibitory conditioned stimuli on the animals with a weak inhibitory process can, evidently, have an unfavorable influence in some cases. However, daily ascents of the dogs Bars and Ryzhii to an altitude of 6,000 m showed that the unfavorable effect of rarefied air may be reduced as a result of high-altitude adaptation not only in a dog with strong, balanced and mobile nervous processes but also in an animal with weaker and more inert inhibition.

The data which we have presented was subsequently confirmed by a number of authors and by us with the aid of the method of conditioned salivary-defense reflexes to acid in experiments on animals (Sulimo-Samuillo, 1955; Zvorykin, Bobrovnitskii et al., 1956) and in investigations

on human beings (Mil'shtein, 1953), which also showed some typological and individual characteristic changes in conditioned reflexes at different altitudes. A comparison of the results of all these papers shows, however, that despite the regular changes at high altitudes common to all reflexes studied there are also, as pointed out by M. P. Brestkin (1956, 1958) specific features characteristic of each type of reflex. Thus, the nature and degree of changes in different conditioned reflexes depend primarily on the biological significance of various conditioned- reflex reactions, characteristic, for example, of alimentary reactions, defense, secretory, motor reactions, and others, as well as natural and artificial reactions. As a rule, conditioned reflexes of direct significance for preservation of life under the given conditions (motor defense, respiratory, cardiovascular, and particularly natural reflexes) are impaired later and less intensely and, conversely, are regained earlier and more completely. It may be supposed that this is brought about not so much by different strengths of the corresponding temporal connections in the cerebral cortex, as by characteristics of reactions providing for preservation of life under threatening circumstances, which have been reinforced by evolution. Thus, unlike the other reflexes which may be studied separately, conditioned alimentary reflexes, which at high altitudes usually are impaired early and recovered late cannot reflect the entire variety of high- altitude changes in higher nervous activity, even though they can reflect general functional changes in higher nervous system centers. Therefore, for a more complete and accurate characterization of the typological nature of high- altitude reactions it is essential, first of all, to consider the specific property of various conditioned reflexes; secondly, to determine the type of nervous system, making use of the same method as is utilized in the study of higher nervous activity at an altitude, and, thirdly, to study heterogeneous conditioned reflexes on the same animals.

Conclusions

1. The nature and degree of changes in higher nervous activity of dogs under the influence of rarefied air and anoxia depend, among other factors, on the type of nervous activity of the animals. This fact explains a number of behavioral differences under these conditions, and may be considered in understanding some characteristics of the reactions of different persons under the influence of altered barometric pressure.

2. Under these conditions, conditioned reflexes change least and are most completely and rapidly recovered in dogs with strong, balanced and mobile nervous processes in the cerebral cortex and with a high functional limit of the cerebral cortical cells. In dogs with a low cerebral cortical functional limit the conditioned reflexes change most and are least completely and least rapidly recovered.

3. In animals with a weak inhibitory process or with inert nervous processes a predominant and even greater weakening of the inhibitory process or of mobility of excitation and inhibition occurs.

4. In the case of high- altitude adaptation a reduction in the disorders of higher nervous activity may occur and there may be an improvement in the recovery of conditioned reflexes in animals with different types of nervous activity.

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THE EFFECT ON HIGHER NERVOUS ACTIVITY OF DOGS OF ACUTE HYPOXEMIA PRODUCED BY RAREFACTION OF THE ATMOSPHERE TO AN ALTITUDE OF 18,000 METERS

(Vliyanie ostroi gipoksemii, vyzvannoi razrezheniem atmosfery do vysoty 18,000 m, na vysshuyu nervnuyu deyatel'nost' sobak)

Most studies of higher nervous activity of animals during hypoxemia have made use of the classic conditioned salivary reflexes. This applies to a number of studies made by co-workers of M. P. Brestkin, in whose laboratory this problem was worked out systematically (Livshits, 1949; Zvorykin, 1951, 1953; Sulimo-Samuillo, 1955; Airapet'yants and Gazenko, 1947) and to works of other authors (Malmejac and Plane, 1952, 1954; Akhmedov, 1954). All these investigations showed that under the influence of an oxygen deficiency, deep-seated, early and prolonged disorders of conditioned salivary reflexes occurred. Hence, it would appear that under these conditions there are corresponding disorders of higher nervous activity as a whole. However, during the course of the subsequent work done by M. P. Brestkin and co-workers, facts began to accumulate attesting to different stabilities of the various conditioned reflexes, worked out on the basis of different unconditioned stimuli with respect to unusual external influences and the discrepancy between changes of a number of conditioned reflexes and the behavior of dogs. As has been determined, conditioned salivary-defense reflexes to acid under unusual influences are, on the whole, more stable than alimentary reflexes. After the effect of acute oxygen deficiency caused by rarefaction of the atmosphere to an altitude of 18,000 m, the conditioned motor-defense reactions to the experimental situation are regained much earlier than the conditioned natural and alimentary reflexes (Vinokurov, 1958). In these experiments it was found that the high-altitude experimental situation alone, with repetition causes a marked inhibition of natural alimentary conditioned-reflexes.

In the work by B. M. Savin and Z.K. Sulimo-Samuillo (1958) it was determined that after the effect of radical accelerations (8—10 g) on the body the acid salivary conditioned reflexes are inhibited, whereas the autonomic component of the reflex is fully maintained.

V. V. Boriskin and V. V. Rassvetaev (1958) found that conditioned salivary defense reflexes to acid were much more stable in the presence of seasickness than were conditioned alimentary reflexes.

Generalizing on all this material, M. P. Brestkin (1958) concluded that extensive evaluation of the condition of higher nervous activity in animals

was unjustified simply on the basis of changes in conditioned reflexes of the digestive glands. He advanced the idea that the stability of various conditioned reflexes under the influence of unfavorable environmental factors is determined by their biological significance for the body when subjected to unusual conditions.

The main aim of the present work was a study of the characteristics of change in higher nervous activity and behavior of dogs during high-altitude experiments under conditions where the vital significance of the alimentary reactions had been increased artificially.

Method

The experiments were performed on four dogs. Repeated, at intervals of 3—4 days, the animals were exposed to the effect of rarefaction of the atmosphere to 56 mm Hg which corresponds to an altitude of 18,000 m. Ascents to altitude were carried out in a pressure chamber, 0.34 cu. m in volume, with a glazed door, which provided a good view and allowed photographs and motion pictures to be taken. The ascent took 12—13 sec; the animals were left at an altitude of 18,000 m for 90 sec. The condition of higher nervous activity was evaluated by the behavior of the animals, which was described in detail and documented by a motion picture.

In accordance with the problem posed, the methods of our experiments were mainly characterized by the fact that in some cases the animals were fed during the period of the experiments, as always, in a vivarium located in a separate building near the laboratory; in others, they received all their food in the chamber in which the ascents were carried out. This condition was observed very strictly, and the experimental animals were not given food anywhere else. In both cases the feeding was conducted once a day, at 3—4 p. m. The animals were raised to altitude on a fasting stomach in the morning hours. They were first adapted to the experimental situation for no less than 10 days. During this period a careful study was made of the behavioral characteristics of the dogs: the relationship to the experimentors and laboratory technicians, to other persons and other animals, reactions to petting, danger, the effect of painful, audio, and photic stimuli, the presence of certain complex conditioned motor reflexes (presenting the paw on the experimentor's request, standing on the hind legs at the command "Beg!"), reactions to various food stimuli (bread, raw and cooked meat, gruel, milk), and others. These reactions were subsequently checked in the performance of the experiments.

Results of the Experiments

Rarefaction of the atmosphere corresponding to an altitude of 18,000 m exerted a marked effect on dogs kept under ordinary vivarium conditions and on dogs fed in the pressure chamber only. Several seconds after reaching altitude the dogs developed opisthotonos, and generalized convulsions occurred, accompanied by marked extension of the limbs and not uncommonly by defecation and urination. The convulsions were

replaced by a general relaxation of the animal's body; in some dogs convulsions occurred repeatedly, but in all cases muscle atony developed at the end of the stay at altitude. The respiration assumed an agonal nature: separate, deep and slow inspirations occurred with the dog's mouth opening wide and the cervical musculature contracting. In a number of cases respiration practically stopped, and for the last 20—30 sec that the dogs were at altitude not a single inspiration occurred. After the descent complete relaxation of the musculature of the animals and the absence of reflexes to all stimuli were noted. Then various convulsive inspirations occurred; they gradually increased in frequency and assumed a rhythmical character. Shortly after, the pupils reacted to light, followed by positive corneal reflex. After this the animals frequently developed opisthotonos and locomotor movements of the limbs. Subsequently, respiration assumed its ordinary character; the dogs began to react to audio and photic stimuli, raised their heads and made attempts to stand on their paws and move about.

Our observations of higher nervous activity of dogs and of their behavior refer essentially to this period.

The experiments showed that in animals given ordinary care and fed in the vivarium, pronounced motor defense reactions to the high- altitude experimental situation appeared as early as after the first ascent. Previously, the dogs, adapted to the experimental situation, walked about independently in the chamber, jumped in it and eagerly took various kinds of food. The same dog, after the first ascent, attempted to leave the chamber and the laboratory and showed active resistance when attempts were made to put it into the chamber, even when motor activity had just begun to return after very severe hypoxemia.

The conditioned motor- defense reflex which occurred showed itself to be quite strong from the very beginning. It was maintained when the behavior of the dog, after descent from altitude, had become completely normal: on the street the dog behaved absolutely the same way as before the high- altitude experiment, played, and was affectionate to the experimentor. However, as soon as it was brought into the laboratory and put into the chamber, a marked change in behavior occurred: it showed active resistance, and when attempts were made to put it into the chamber it even showed aggressive reactions. On subsequent ascents this reaction became progressively more pronounced and was induced by progressively more distant conditioned- reflex stimuli. The dog began to show resistance even when it was brought to the doors of the laboratory and subsequently began to react negatively to the laboratory technician who had come to the vivarium to get it.

This data was obtained on two dogs, which were subjected to the effect of rarefaction under ordinary conditions of care and feeding in the vivarium.

A completely different picture was obtained when the animals were fed only in the pressure chamber for a long time (1—2 months) before the ascents. Under these conditions the dogs very quickly developed pronounced positive reflexes to the chamber, the laboratory, and the laboratory technician who came to take the animal for a routine feeding.

Thus, the dog Lisa, following a 50- day feeding period in the chamber, began to react warmly and vigorously to the entrance of the laboratory technician into the vivarium, and once released from its cage, it ran headlong into the laboratory building, toward the chamber where the food had been prepared, jumped into the chamber by itself and began to eat.

The first ascent to an altitude of 18,000 m under such preliminary conditions was accompanied by no less troublesome phenomena in these dogs than in animals which had been cared for as usual. However, after the descent their behavior was entirely different. After the high-altitude experiment, as soon as motor activity had returned to them, these dogs did not show any signs of defensive reactions to the experimental situation or the pressure chamber. Conversely, they went toward the chamber in an attempt to jump into it even when they showed pronounced lack of coordination of movements and the inability to maintain a normal body position.

Repetition of the ascents, with the animals still receiving all their food in the pressure chamber, did not change the situation for practical purposes. In the dogs Lisa and Kashtan, following nine ascents to an altitude of 18,000 m, the same definitely positive reflexes were shown to the high-altitude experimental situation and to all the stimuli preceding it (entrance of the laboratory technician into the vivarium, the walk to the laboratory).

During the course of this work a study was made of the behavior of the same four animals when the experimental conditions were changed. Some dogs (Ryzhik and Chernysh) were first exposed to the effect of a rarefied atmosphere under ordinary feeding conditions, were then shifted over to feeding in a pressure chamber, and after a 1.5—2 month period again were repeatedly exposed to the effect of altitude. Others (Lisa, Kashtan) conversely, initially were fed only in the pressure chamber for 1—1.5 months, and under these conditions were exposed (as many as 10 times) to the action of rarefaction of the air; then they began to receive their entire diets in the vivarium, and after at least a month were again exposed to repeated high-altitude effects. In all cases the same result was obtained: if the dog was fed in the pressure chamber only, this latter, like all preliminary stimuli, failed to produce any negative reaction either after the ascents or in the intervals between them; if feeding of the dog was conducted in the ordinary way — in a vivarium — in every high-altitude experiment and in the interval between them, the dog showed definite resistance to all manipulations associated with the experiment.

It goes without saying that with a change in the feeding conditions the changes of the dogs' behavior did not occur immediately but gradually. Thus, the animals exposed to high-altitude experiments when fed in the ordinary way in a vivarium did not take food when they were shifted over to regular feeding in the chamber but ate only in the street, and then in the laboratory, but only outside the chamber; finally, after 4—5 days they did eat inside the chamber. In accordance with this, there was a change in their reactions to various stimuli accompanying the experiments and in their behavior. Likewise, the dogs which took food initially only in the pressure chamber and showed no negative reactions to the situation of the high-altitude experiments, despite frequent repetitions of them, began to show a definite negative reation to the entire experimental procedure when they were shifted over to feeding in a vivarium after only one or two ascents.

The facts presented are illustrated by the motion-picture frames shown in the figures.

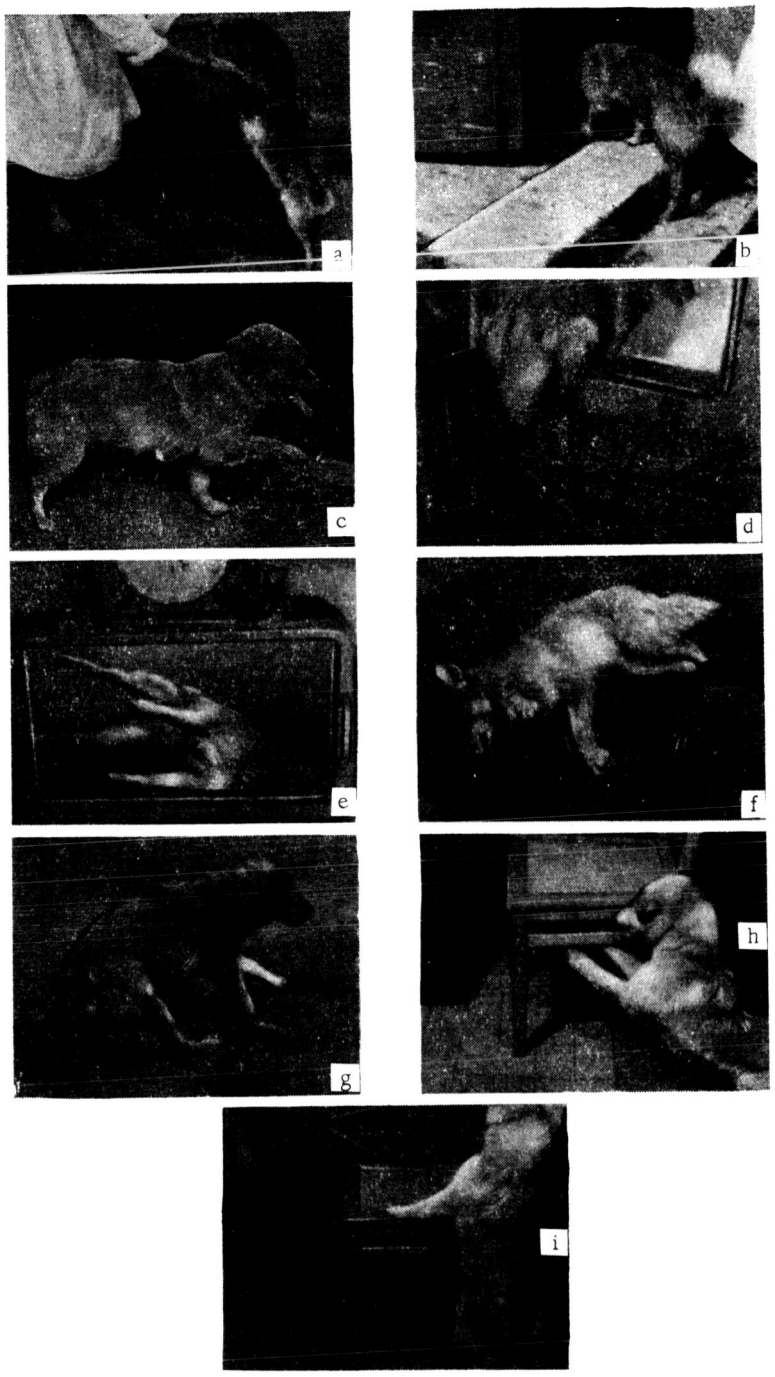


FIGURE 1. Motion-picture frames showing the behavior of the dog Ryzhik under ordinary feeding and vivarium conditions. First high-altitude experiment. Explanation in the text.

In Figure 1 the behavior of the dog Ryzhik is shown during the first experiment with ascent to an altitude of 18,000 m under ordinary feeding and vivarium conditions. Before the experiment, during the walk, the dog played with the laboratory technician (Figure 1, a) and went without force into the laboratory (Figure 1, b); near the pressure chamber it behaved quietly, and on the experimenter's request it gave its paw (Figure 1, c) and jumped independently into the pressure chamber (Figure 1, d).

After 35 sec of being at an altitude of 18,000 m, the dogs developed generalized convulsions (Figure 1, e); in the 65th second these stopped, and general atony developed; respiration became periodic and superficial. Figure 1,f reflects the condition of the dog 40 sec after descent to the ground. Reflexes were absent to all stimuli; the animal's body relaxed; respiration became slow and of the convulsive type, The dog stood on its legs 22 min after the ascent, was brought out onto the street, and marked ataxia was noted (Figure 1, g — 23 min after descent). In the laboratory, 25 min after descent, the dog showed active resistance when attempts were made to put it into the pressure chamber, although coordination had not yet been completely restored.

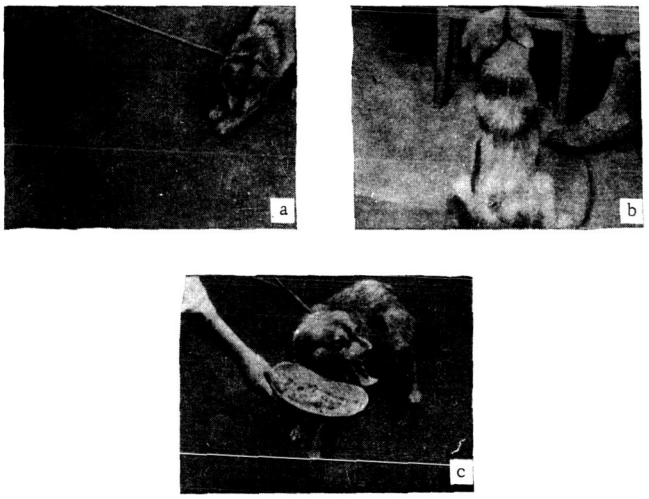


FIGURE 2. The same as Figure 1. Ninth high-altitude experiment

As the result of subsequent ascents the motor defense reflexes just noted in the dog Ryzhik began to be more pronounced. In Figure 2 it is shown that in the ninth high- altitude experiment the dog resisted going into the laboratory building (Figure 2, a) and into the pressure chamber (Figure 2, b) and refused the food offered near the pressure chamber (Figure 2, c). After this experiment the ascents were temporarily stopped, and for 1.5 months Ryzhik was given food in a pressure chamber rather than in a vivarium. Figure 3 reflects the behavior of the dog in the first high- altitude experiment after this change in conditions. During the walk Ryzhik was affectionate and playful (Figure 3, a), went into the laboratory

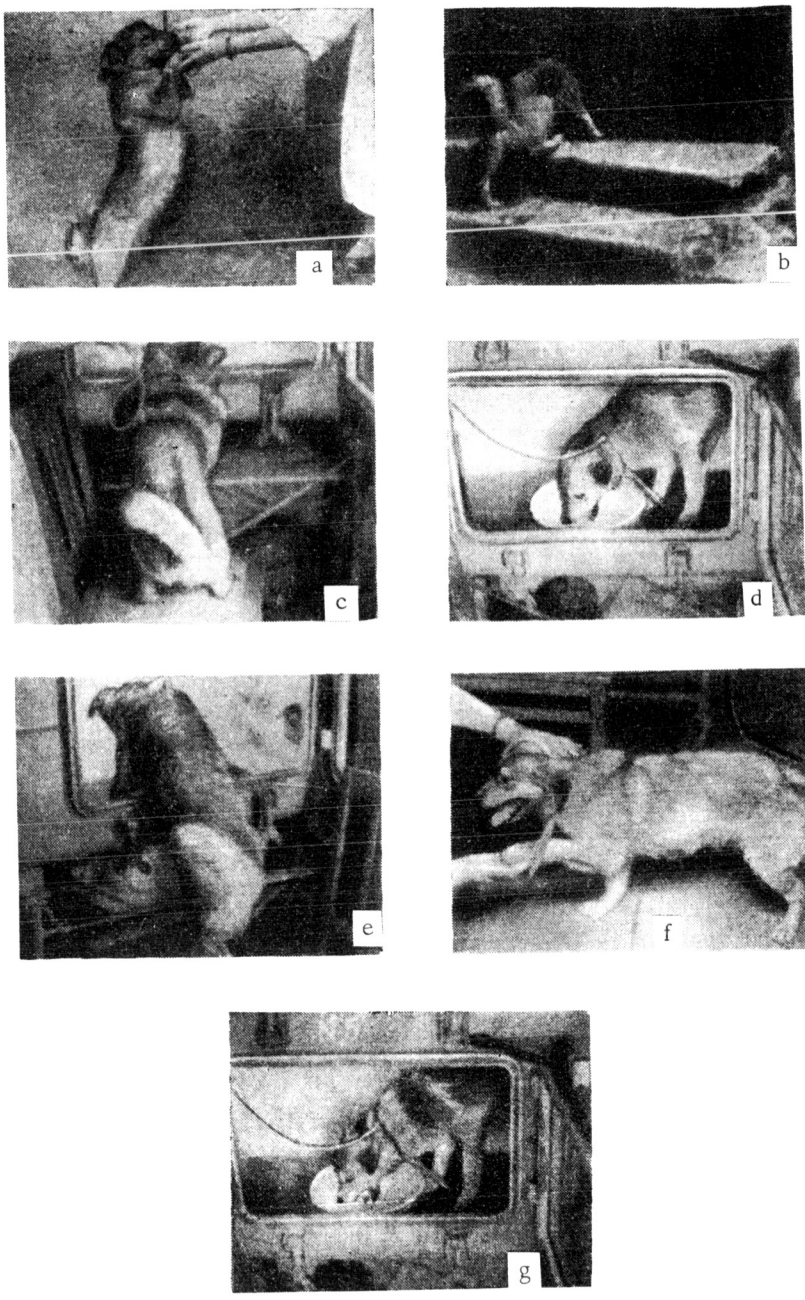


FIGURE 3. Motion-picture frames reflecting the behavior of the dog Ryzhik 1.5 months after regular feeding in the pressure chamber. First high-altitude experiment. Explanation in the text.

independently (Figure 3, b), jumped into the chamber (Figure 3, c) and eagerly ate its food supplements (Figure 3, d). Thirteen minutes after the descent from an altitude of 18,000 m, the stay at which was accompanied by the usual severe phenomena and development of a preagonal state, Ryzhik, despite pronounced ataxia, independently got up on a chair and went into the pressure chamber (Figure 3, e). After 15 min outside the chamber it presented its paw (Figure 3, f), and after 17 min it eagerly ate meat inside the chamber (Figure 3, g).

After this experiment, under conditions of being fed in the pressure chamber only, Ryzhik was exposed to the action of rarefaction another five times but despite this, did not lose its positive reflexes to the experimental procedure or to the pressure chamber. In Figure 4 its behavior is shown in an experiment with the sixth ascent to altitude under conditions where it was fed in the chamber only. As the figure shows, during the walk the dog was affectionate and playful (Figure 4, a), and behaved as usual in the laboratory near the chamber: it offered its paw (Figure 4, b), and, on the command of the experimenter, it independently and immediately jumped up onto the chair and into the pressure chamber (Figure 4,c,d,e). Immediately after descent from altitude the animal was absolutely prostrate (Figure 4,f); after 8 min it arose shakily on its hind legs; after 10 min it independently went into the pressure chamber, and after 15 min it ate meat eagerly in the chamber (Figure 4, g). It showed no negative reactions to the experimental situation, behaving as usual near the chamber and offering its paw (Figure 4,h — 18 min after descent).

The next series of motion-picture frames (Figures 5, 6, 7, 8, and 9) apply to the dog Lisa, which during the first period of the experiments was given food in the chamber; in the second, in the vivarium; in the third, again in the chamber,

In Figure 5 the behavior of the dog Lisa is shown in the first high-altitude experiment, which was performed after a 2-month feeding of the dog in the pressure chamber only. Before the ascent the animal showed definitely positive reactions to the experimental situation and to the pressure chamber. During the walk the dog played, sat up on its hind legs (Figure 5, a) and then hurried into the laboratory building (Figure 5, b), offered its paw before the chamber (Figure 5, c), sat up on its hind legs and reacted to the food (Figure 5, d), jumped into the chamber by itself (Figure 5, e, f) and eagerly ate ordinary food there (Figure 5, g), and then, while in its harness, behaved absolutely quietly (Figure 5, h).

After 8 min at altitude, convulsions appeared (Figure 5, i), and then complete atony occurred and respiration stopped. Immediately after descent (Figure 5, j) the dog hung lifelessly by its harness. Five min later it came to, and stood on all four legs. Six min after, the harness was removed and after it had been placed on the floor near the chamber it showed pronounced ataxia, but nevertheless got up onto the chair and went into the chamber by itself (Figure 5, l, m); in the 8th minute it drank milk in the chamber (Figure 5, n), offered its paw to the experimenter (Figure 5, o) and then behaved as usual near the chamber without showing any defensive reactions (Figure 5, p).

The dog showed the same behavior in the next eight high-altitude experiments which took place under the same conditions, i.e., with feeding of the dog in the chamber only. In Figure 6, motion picture-frames are shown pertaining to the last, ninth experiment in this stage of the investigation.

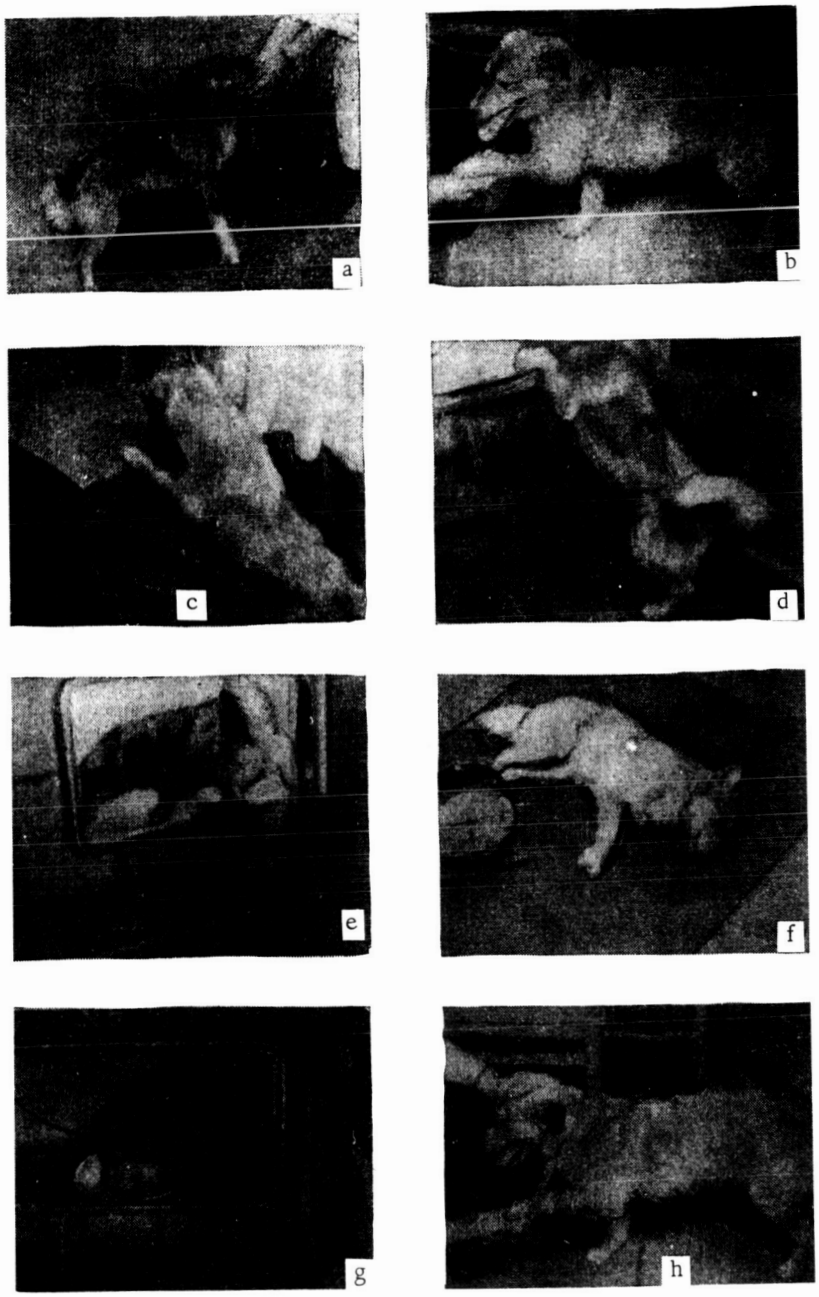


FIGURE 4. The same as for Figure 3. Sixth high-altitude experiment. Explanation in the text.

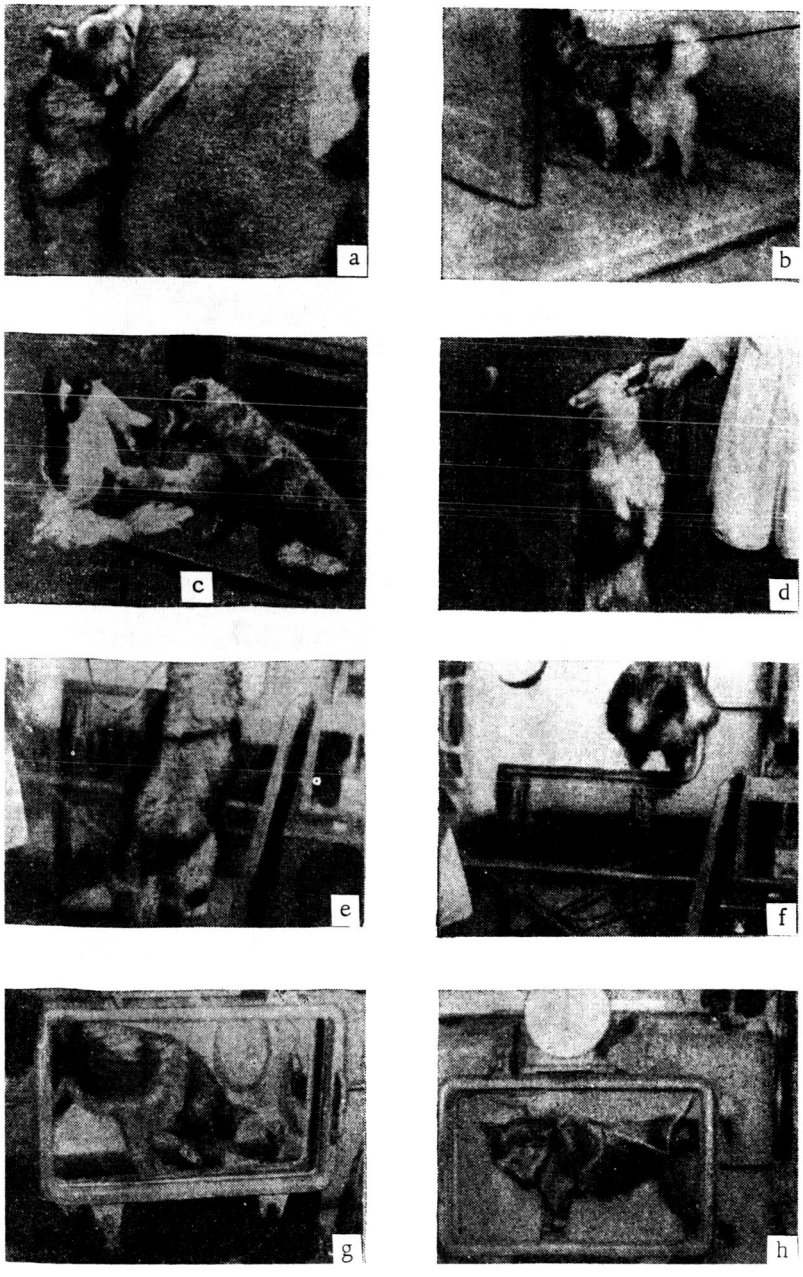


FIGURE 5. Motion-picture frames reflecting the behavior of the dog Lisa 2 months after regular feeding in a pressure chamber. First high-altitude experiment. Explanation in the text.

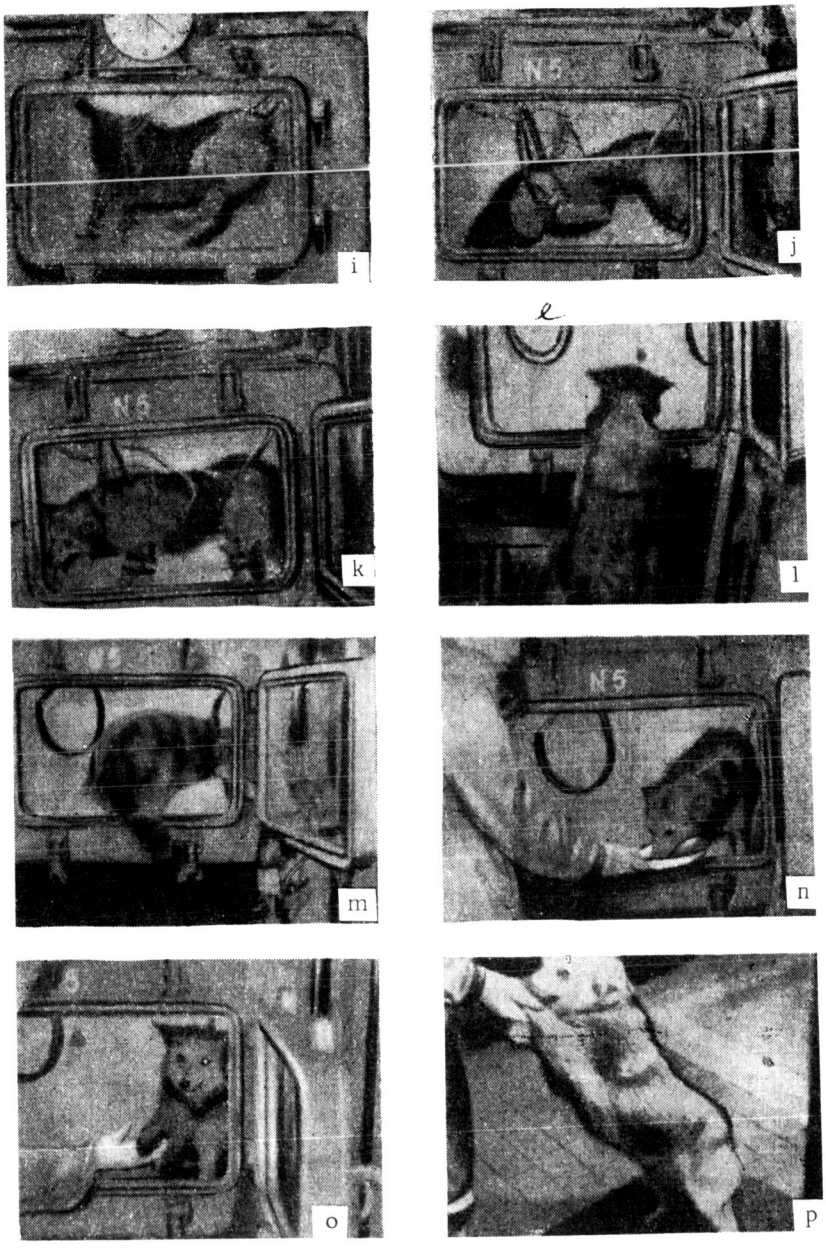


FIGURE 5. (Continuation)

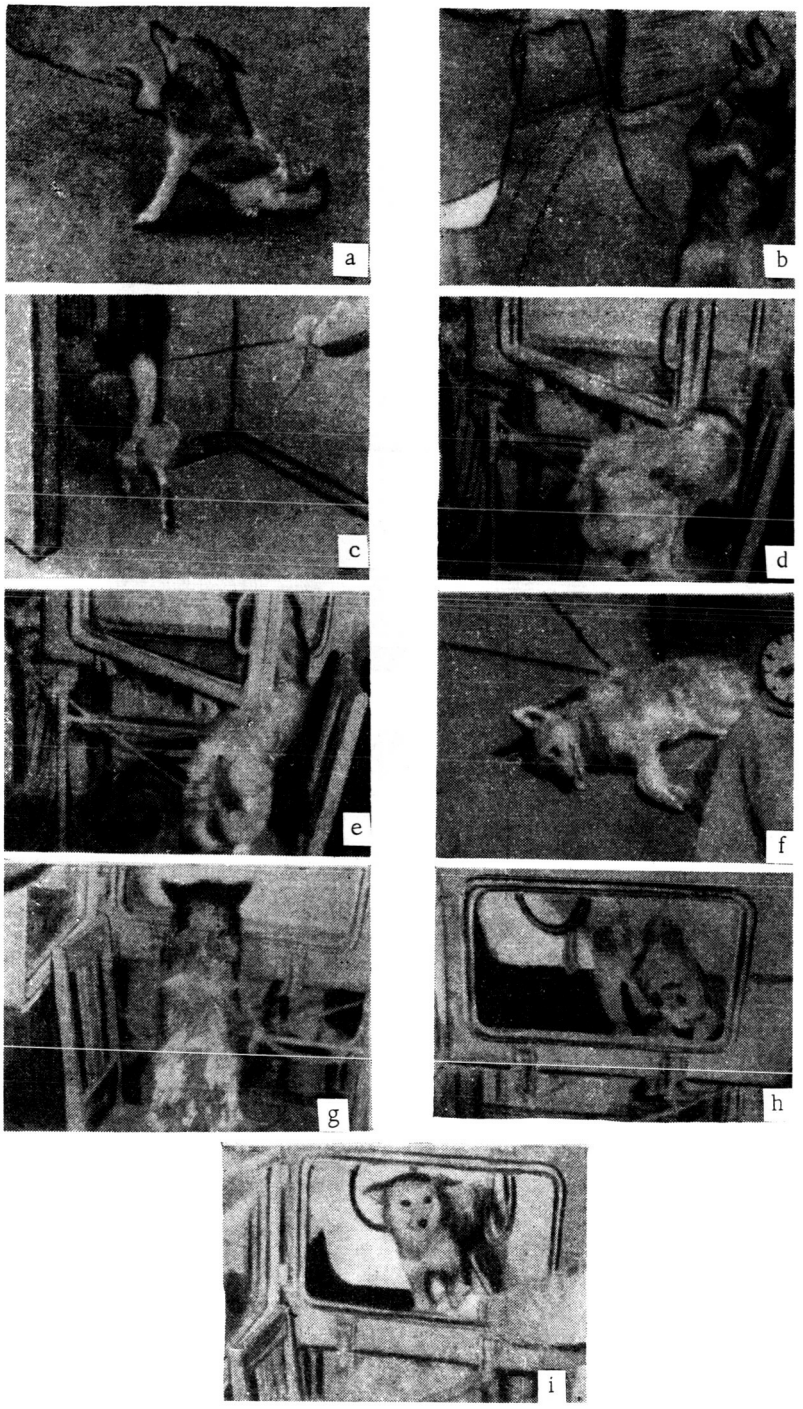


FIGURE 6. The same as for Figure 1. Ninth high-altitude experiments. Explanation in the text.

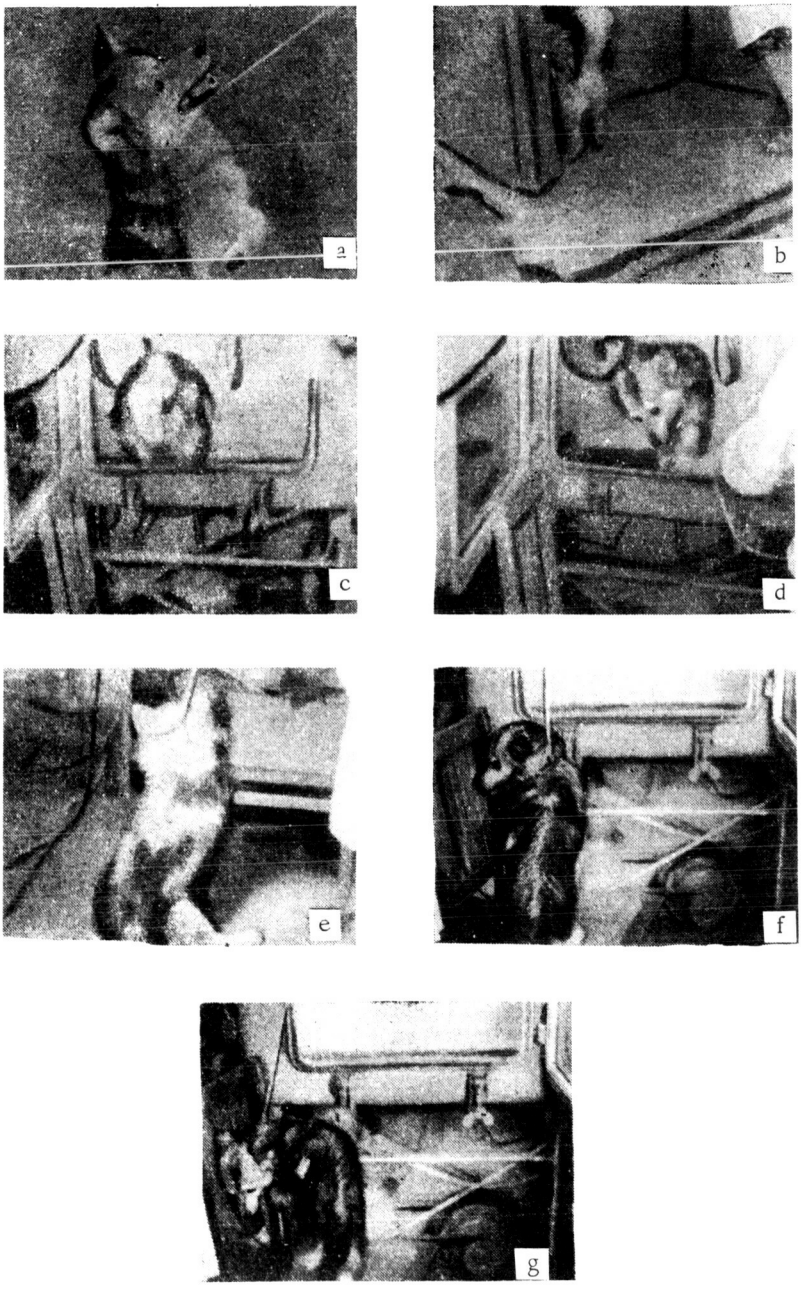


FIGURE 7. Motion-picture frames reflecting the behavior of the dog Lisa, 1 month after regular feeding in the vivarium. First high-altitude experiment. Explanation in the text.

Before the experiment the dog was playful and frisky (Figure 6, a, b), ran to the laboratory (Figure 6, c), toward the chamber, and found its door half open, whereupon it opened it fully and crawled into the chamber (Figure 6, d, e). Immediately after the descent it was completely prostrate, had respiratory arrest and showed no reactions to external stimuli (Figure 6, f). In the 6th minute, stumbling and falling, it crawled onto the stool and into the chamber (Figure 6, g); in the 9th minute it drank milk there (Figure 6, h) and subsequently remained quietly in the chamber (Figure 6, i).

After this, the experiments with ascents were stopped; the dog began to be fed in the vivarium as usual, and after a month it was again used in the experiment. As is shown in Figure 7, the dog's behavior before the ascent remained as previously (Figure 7, a, b, c, d); however, after it, as early as in the 6th minute, after having just returned to consciousness, the animal showed motor defense reactions (Figure 7, e, f, g).

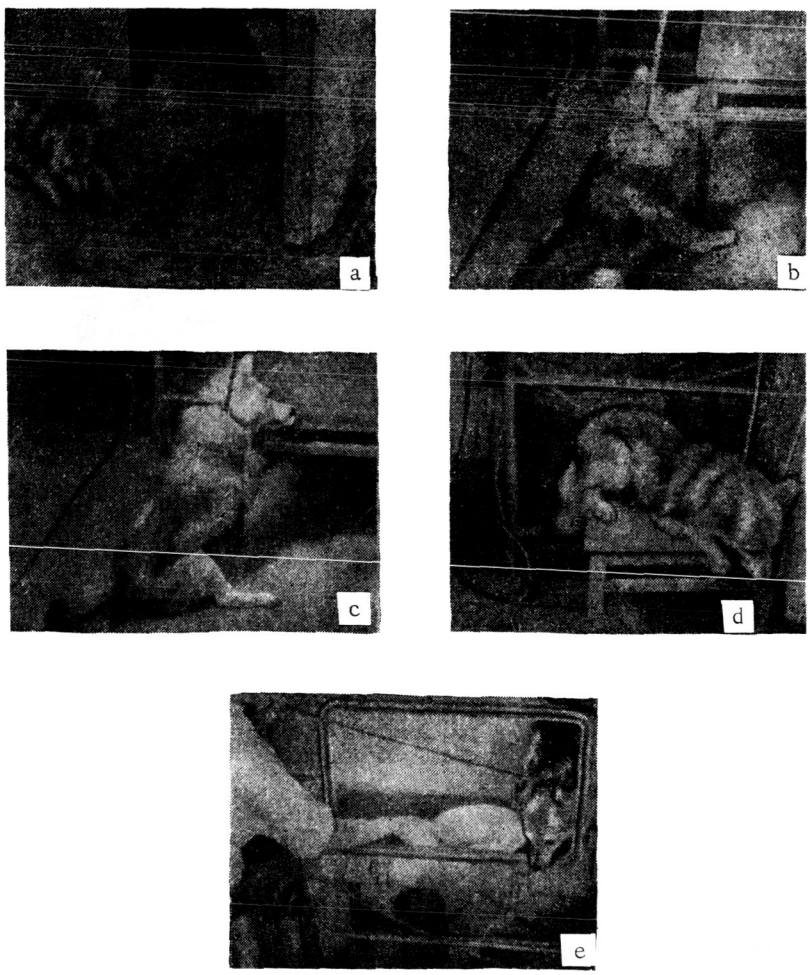


FIGURE 8. The same as for Figure 7. Fourth high-altitude experiments.

As the result of the next two ascents under conditions of constant feeding in the vivarium, the dog's reactions were increased and reinforced. In the fourth experiment (Figure 8) the dog would not go into the laboratory (Figure 8, a), showed resistance when brought close to the chamber (Figure 8, b, c), attempted to run away from it (Figure 8, d), and refused meat and milk in the chamber (Figure 8, e). Then high-altitude experiments on the dog Lisa were again stopped for a month, during which time the dog again began to be fed only in the chamber. The negative reactions to the experimental situation and to the chamber were very quickly replaced by positive reactions, and these latter remained, despite seven ascents to an altitude of 18,000 m, in which the animal was brought to an agonal state every time.

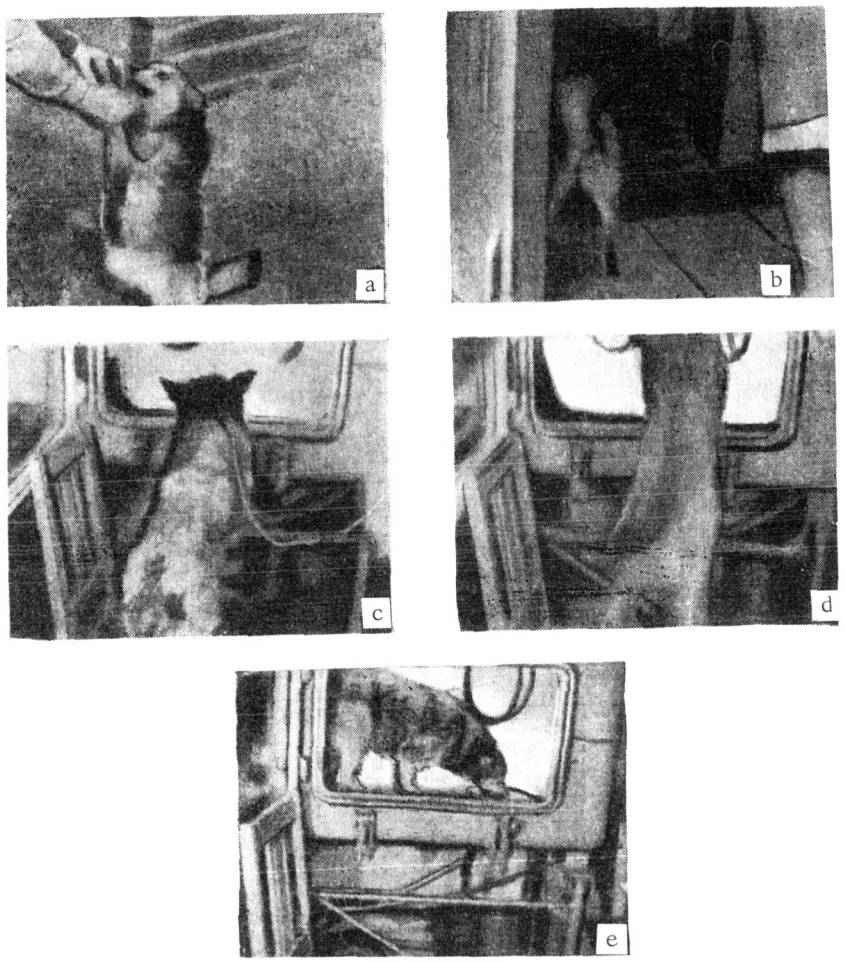


FIGURE 9. Motion-picture frames depicting the behavior of the dog Lisa 1 month after second period of regular feeding in the pressure chamber. Seventh high-altitude experiment. Explanation in the text.

The behavior of the dog Lisa in the seventh high- altitude experiment of this last stage of the investigations is shown in Figure 9. As in the original experiment, the dog played when it was taken for a walk (Figure 9, a), ran to the laboratory (Figure 9, b), and jumped into the chamber (Figure 9, c); after the ascent it again ran to it as soon as it acquired capacity of locomotion which was still far from complete (Figure 9, d), and after several minutes more it drank milk in the chamber (Figure 9, e).

Therefore, experiments on the dog Lisa showed that repeated change in feeding conditions resulted every time in change in the animal's behavior in the experiments and in its reactions to the chamber in which ascents to altitude were carried out.

Discussion of Results

The experiments performed completely confirmed the idea advanced by M. P. Brestkin that the stability of conditioned reflexes in the presence of strong external factors is determined by their biological significance for the organ experiencing unusual effects. This was shown in a very striking manner in our experiments through the example of natural reflexes to food. Before the experiments with ascents to altitude all the dogs reacted in a lively manner to various foodstuffs offered them in the laboratory near the chamber and inside the chamber, and eagerly ate the food. Natural alimentary reflexes in this situation were, therefore, present in all the animals, regardless of where they had been constantly fed. However, as early as after the first ascent the situation became absolutely different for dogs fed in the vivarium and those fed in the chamber. In the first case, as the result of acute hypoxemia, natural alimentary reflexes were lost, the animals refused food not only in the immediate period after the descent but also subsequently, with complete restoration of functions. Moreover, in these animals the alimentary reflexes in the given situation were absent or were markedly inhibited even in the days following the ascent. In the latter case, in dogs fed regularly in the chamber, the alimentary reflexes were inhibited under the influence of hypoxemia for only a very short time, corresponding to the period of severe functional disorders. As early as several minutes after the dog, taken out of the chamber and returned to consciousness, had regained its ability to stand and move about, it began, as previously, to react in a lively manner to food stimuli and ate the food supplements. Under the influence of the experimental situation no changes were observed in the natural alimentary reflexes in these animals on subsequent days. These differences in reflexes which are essentially the same were undoubtedly connected with their different biological significance under the given conditions for dogs feeding in the vivarium and for dogs feeding in the chamber. For the former, alimentary reflexes in the given situation were connected, by and large, only with episodic feeding, of no vital importance to the body; for the latter these reflexes under the same conditions were associated with the nutrient function, representing one of the main conditions for life. Undoubtedly, this fact determines the entire behavior of the dogs, both in the immediate period after acute hypoxemia and on subsequent days. In animals which had been given food in the vivarium, as early as the first high- altitude experiment there were

pronounced defensive reactions to the circumstances in which the hypoxemic factor operated. It is significant that these conditioned-reflex connections are formed during the development of the most severe anoxia, when there was a definite disorder of the general condition of the body and an undoubted change in the condition of the cerebral cortex. Nevertheless, the conditioned reflexes formed were very stable and were maintained firmly in the days following the ascent.

In animals which had been given all their food in the chamber in which they had been exposed to the effect of hypoxemia, no defense reflexes to the high-altitude experimental situation developed. On the other hand, these dogs, even long before complete recovery of the hypoxemic functions which had been impaired, showed consolidated positive reactions to the given situation based on feeding in the chamber. Again, this is associated with the prime vital significance of the nutrient function; the reflexes pertaining to it, directed toward its fulfillment, are predominant even under those unfavorable conditions resulting from ascent to altitude.

It is very interesting that under the influence of acute anoxia, positive motor reactions of animals directed toward the food, elaborated by feeding them in the chamber, were more persistent that the eating process itself. After descent from altitude the dogs first showed a tendency to go toward the chamber, although they still refused food offered. A positive reaction to food usually appeared several minutes after the positive motor reaction to the sight of the chamber. It is possible that we are dealing here with the predominant depression of the digestive function under the influence of hypoxemia. As has been pointed out by M. P. Brestkin (1958), one of the main principles in the body's reaction to unusual conditions, particularly to an oxygen deficiency, is the mobilization of the inner reserves of the body: an increase in the activity of those systems which assure compensation of harmful influences, through simultaneous inhibition of the activity of other systems which have no direct relationship to the compensatory reaction.

The digestive apparatus appears precisely as a system in which activity may be temporarily depressed to allow for more complete development of protective reactions, under the influence of a number of unfavorable effects, particularly hypoxemia. Evidently, this is why, after descent from altitude, there is a discrepancy between the time of appearance in dogs of positive general motor reactions to the chamber and of positive reactions to food, directly associated with the actual act of eating. However, the overall behavior of the dogs under these circumstances is not determined by these reactions of conditioned alimentary reflexes in the narrow sense, but rather deep-seated conditioned-reflex connections dealing with the nutrient process of the body as a whole.

Conditioned-reflex changes in respiration and cardiac activity of the animals associated with hypoxemia deserve special attention. Conditioned-reflex dyspnea and tachycardia prior to repeated ascents to altitude occur not only in dogs fed in the vivarium. On being put in the chamber there are definitely negative reactions to the high-altitude experimental situation; these reactions remain in animals fed only in the chamber, which have shown no negative reflexes to preparation for the next ascent. Therefore, very unique relationships obtain: on the one hand, hypoxemia cannot depress the positive general and food reactions elaborated on the basis of

feeding the dogs in the chamber; on the other hand, these reactions, which determine the behavior of the animals under the given conditions, do not exclude the formation of conditioned reflexes directed at the control of the hypoxemic state.

Conclusions

1. Under ordinary feeding conditions of dogs in a vivarium, their ascents to an altitude of 18,000 m in a pressure chamber, leading to the development of marked hypoxemia, are accompanied by the rapid formation of motor defense conditioned- reflex reactions to the experimental situation, and complete inhibition of the natural reflexes to food.

2. After 1—2 months of being only in the pressure chamber, the animals maintained positive reactions to the experimental situation and to food stimuli, despite subsequent repeated ascents in this chamber to the same altitude, accompanied every time by a most severe anoxia.

3. The higher nervous activity characteristics and behavior of dogs observed are underlain by different degrees of stability of conditioned reflexes depending on their degree of biological significance in the presence of unusual environmental factors.

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THE DEVELOPMENT OF DINITROPHENOL-INDUCED HYPERTHERMIA UNDER ALTERED PARTIAL PRESSURES OF OXYGEN AND CARBON DIOXIDE

(Razvitie dinitrofenolovoi gipertermii pri izmenennykh partsial'nykh davleniyakh kisloroda i uglekisloty)

In the study of experimental hyperthermia, 2—4—dinitrophenol (DNP) has been widely used. Its administration results in intense hyperthermia and a considerable increase in the oxygen consumption. According to the generally accepted opinion (Il'in and Neifakh, 1956; Veselkin, 1960; Zdorovskaya, 1960), the effect of DNP is connected with dissociation of respiration of oxygen and phosphorylation, and a breakdown of macroergic compounds, mainly in the liver and muscles.

A comparison of the data of direct and indirect calorimetry in experiments with DNP administration performed in the laboratory of P. N. Veselkin showed a considerable discrepancy between heat production and oxygen consumption. In the first period of the experiment excess heat production occurs with respect to oxygen consumption; in the second period, conversely, the actual heat production lags behind that calculated in accordance with the oxygen consumed and the carbon dioxide produced (Zykina-Gramenitskaya, 1960).

From the papers of P. M. Al'bitskii (1884, 1885, 1904, 1911), E. A. Kartashevskii (1906) and N. V. Veselkin (1913) it is well known that variations in the oxygen and carbon dioxide contents of the body have a direct bearing on the course of metabolic processes and an essential influence on the heat balance of the body.

In the present work we decided to study the development of DNP-induced hyperthermia under altered partial pressures of oxygen and carbon dioxide, calculating that the data obtained would be useful for the analysis of the toxic effect of oxygen.

Method

The experiments were performed on rabbits of both sexes weighing 1.5—3.5 kg.

To induce hyperthermia the DNP solution was injected into the auricular vein in a dose of 0.02 g/kg immediately before the use of one procedure or another. During the course of the experiment the animal's body temperature was measured with a maximum rectal thermometer or a rectal thermocouple or mirror galvanometer.

For the purpose of studying the influence of reduced partial oxygen pressure in experimental animals immediately after DNP administration, they were raised to a height of 5,500 m in a vacuum chamber, where they were kept for an hour; after this they were lowered to ground level. The ascent and descent were always conducted at the same rate (30—35 m/sec). in all experiments the temperature in the vacuum chamber was 20—25°.

In the study of the effect of hyperoxemia following DNP administration the rabbits were placed in a compression chamber where, after preliminary ventilation with oxygen, oxygen pressure was increased to 4 atm. In the majority of experiments the animals were under an atmosphere of compressed oxygen for 5, 10, or 12 min.

An investigation to the effect of hypercapnia on the development of DNP- induced hyperthermia was made in an airtight chamber, in which a gas mixture of 20% carbon dioxide and 40% oxygen was created; the animals remained in this chamber from 30 min to 1 hr, depending on their conditions.

To induce hypocapnia after a preliminary tracheotomy the rabbits were subjected to prolonged intense pulmonary ventilation by means of bellows. In these experiments the animals were tied down to the table in the usual way; in all others, they were left free.

The control experiments were as follows: study of the development of DNP- induced hyperthermia under ordinary conditions; study of body temperature under altered partial oxygen and carbon dioxide pressures without preliminary DNP administration; and, finally, recording of the rectal temperature during hypoxemia, hyperoxemia, hypercapnia and hypocapnia, after preliminary injection of a 0.7% solution of sodium bicarbonate, which is a solvent of DNP

In the control experiments thermometry was performed every 15 min for 1.5—2 hrs; in vacuum chamber experiments, before and after the procedure, and then every 15 min; experiments using hyperventilation, every 5 min.

In all experiments the conditions of the animals were constantly observed.

A total of 77 experiments on 63 rabbits was performed.

Results of the Experiments

Intravenous DNP injection into rabbits (0.02 g/kg under ordinary conditions always produced a pronounced hyperthermic effect. In one hour the increase in rectal temperature reached 0.8—2.5° (Table 1). As a rule, the condition of the animals was not disturbed. In most cases dyspnea was observed [sic]. It should also be noted that the most pronounced hyperthermic effect from DNP injection is observed in young animals.

In a number of cases (9 out of 77) DNP administration alone resulted in death shortly afterwards.

Cutting the partial oxygen pressure in the inhaled air by half, which occurs in the ascent to an altitude of 5,500 m*, prevents the development

* At an altitude of 5,500 m the partial pressure of oxygen is about 85 mm Hg, that is, half of ordinary atmospheric pressure.

of DNP-induced hyperthermia (Table 2). Under these conditions, the body temperature of most of the animals even dropped. Cases of a very slight increase (no more than 0.2—0.4°C) are noted with an increase (between 1—4 min) in the interval between the injection of DNP and the ascent. Intact control rabbits raised to altitude show an even greater decrease in rectal temperature than animals which had first received DNP (Table 3). Injection of a 0.7% sodium bicarbonate solution in the same volume as the DNP solution before the ascent prevents cooling (Table 3). This is evidently associated with increased alkalinity of the blood, limiting the "high altitude" dyspnea.

TABLE 1

Change in the rectal temperature (in °C) in rabbits after the injection of DNP

Number of the experiments	Initial temperature	Temperature ranges								Notes
		Time after injection (in min)								
		15	30	45	60	75	90	105	120	Maximum increase
2	38.7	—	—	39.6	—	—	40.1	—	—	+1.4	
3	38.9	—	—	—	39.7	—	—	—	—	+0.8	Rabbit tied down on a stand (death after 1 hr)
4	39.5	40.0	40.05	—	40.2	40.5	40.25	—	—	+1.0	
25	39.9	—	40.3	—	41.2	—	42.0	—	—	+1.7	
38	39.2	40.4	40.5	40.4	40.4	—	—	—	—	+1.3	Serious condition, dyspnea
75	39.7	40.1	40.5	41.3	41.9	—	42.2	42.0	—	+2.5	Very young rabbit Weight 1,500 g
77	39.2	39.5	39.8	39.4	—	40.9	—	41.5	—	+2.3	Very young rabbit of light weight
17	39.5	39.6	39.8	39.6	39.8	39.9	39.5	—		+0.3	The rabbit had been used in the experiment one day before

Investigation of the effect of increased oxygen pressure on the development of DNP-induced hyperthermia (13 experiments) showed that hyperoxemia causes an exceedingly rapid and intense elevation of the rectal temperature (Table 4). In 5 min (and in 2 experiments, in 10 and 12 min) the increase in body temperature reached 0.8—1.7°. The animals usually died 4—5 min after decompression. During that time the temperature continued to increase, in most cases by 0.1—0.5°. An exception was experiment No. 14, in which in an experimental animal kept under a compressed oxygen atmosphere for 50 min after the DNP injection, rectal temperature failed to increase, but decreased 0.4°. During this time the rabbit was under an increased oxygen pressure of 4 atm without any signs of oxygen poisoning, and one hour after decompression the rectal temperature practically reached the initial level. Apparently, this is associated with the fact that a day before this experiment the rabbit was given DNP, and was twice exposed to the effect of rarefaction in the vacuum chamber.

TABLE 2

Change in the rectal temperature (in °C) in rabbits with ascent to an altitude of 5,500 m after the administration of DNP

Number of experiment	Initial temperature	Interval between injection and ascent (in min)	Period of time at altitude (in min)	Temperature after descent	Increase or decrease in the temperature from the initial	Period of time spent at ground level after descent (in min)				Increase of temperature	Notes
						15	30	45	60		
5	39.2	Immediately	60	38.6	-0.6°	—	39.7		40.0°	+1.4	
6	38.5	3	60	38.7	+0.2	—	40.3	—	40.6	+1.9	
7	40.0	Immediately	60	39.3	-0.7	39.3	40.3	40.7	41.1	+1.8	
8	39.4	2—3	60	39.4	0°	39.7	39.7	40.4	40.7	+1.3	
18	39.6	1	60	39.9	+0.3	40.3	40.5	40.3	40.5	+0.6	
20	40.0	Immediately	60	39.8	-0.2						Beginning with the 20th minute, convulsions; death in measured minute; temperature taken post-mortem
21	39.1	Immediately	30	39.4	+0.4						Death in the 30th minute; temperature measured post-mortem
24	39.3	Immediately	60	37.7	-1.6	38.3	38.45	38.8	39.0	+1.3	
36	39.8	Immediately	5—6	39.85	+0.05						Rapid death; temperature measured post-mortem
40	39.7	4	1	39.8	+0.1						Death; temperature measured post-mortem
41	39.8	Immediately	20	38.7	-0.9						Death in the 20th minute; temperature measured post-mortem
42	39.55	1	60	39.6	+0.05	40.4	40.6	40.4	40.4	+10	post-mortem, +1.0°
49	40.7	Immediately	Death immediately after ascent							(over 30)	
62	39.1	Immediately	20	38.4	-0.7	Death 1 hr after descent					
46	39.4	2	20	39.5	0						Death in the 20th minute; temperature measured post-mortem

TABLE 3

Change in the rectal temperature (in °C) in rabbits in the control experiments with ascent to an altitude of 5,500 m in one hour

Number of experiment	Temperature			
	Initial	After descent	Increase or decrease	After 60 min at ground level
19	40.0	39.1	-0.9	
23	39.8	38.6	-1.2	39.0
34	41.6	37.9	-3.7	38.3
50	39.9	37.2	-2.7	38.7
61	38.7	37.8	-0.9	38.7 (20)
35*	39.3	39.4	+0.1	39.2
37*	38.6	39.3	+1.3	
39*	39.7	39.7	0	
43*	39.3	39.9	+0.6	
45*	39.2	40.0	+0.8	

* Before the ascent a sodium bicarbonate solution was given (0.7%)

TABLE 4

Variations in rectal temperature (°C) in rabbits under increased oxygen pressure of 4 atm after DNP administration

Number of experiment	Initial temperature	Exposure (in min)	After compression	Increase of temperature	Period of observation, to time of death (in min)	Increase of temperature after compression	Bulk increase of temperature	Notes
14	39.2	50	38.8	-0.4	60	-0.6		Was tested twice (altitude + DNP)
15	39.4	Death in chamber after 35 min						
16	38.8	The same						
60	39.2	5	40.8	+1.6	Died before compression			Temperature before repeated action of pressure
66	38.7	5	39.6	+0.9				
67	38.8	12	40.5	+1.7	4	+0.1	+1.8	
69	37.9	5	38.7	+0.8	10	+0.4	+1.2	
70	39.3	10	41.0	+1.7	5	+0.5	+2.3	Indication of oxygen poisoning before compression
72	39.2	5 5	40.5 41.6	+1.3 +1.1	5	0		

In control experiments in which intact animals were put into an atmosphere of compressed oxygen for the same period (5—12 min) a very slight decrease of the rectal temperature was noted (no more than 0.5°).

The injection of DNP causes a marked change in tolerance to rarefaction of the atmosphere and increased oxygen pressure. Ascent to an altitude of 7,000—8,000 m results in marked clonic convulsions of the animal's entire body and death in several seconds; as is well known, this never occurs in normal animals under these conditions. Even at a height of 5,500 m rabbits which have received DNP usually show marked hypoxemic phenomena: cyanosis of the lips and ears, marked dyspnea (as many as 200 respirations per min), marked hyperextension of the head, and loss of motor coordination. In control rabbits at the same altitude practically no appreciable disorders were noted. Rabbits given the sodium bicarbonate solution before the ascent tolerated the effect of rarefaction with somewhat greater difficulty than the intact animals, but with less difficulty than the animals which had first been given DNP.

Under the influence of an increased oxygen pressure of 4 atm marked dyspnea (as many as 180 respirations a minute) was observed in the experimental rabbits immediately upon termination of compression (1—2 min). The respiratory movements were marked, deep, and strained. The animal lay on its side in the chamber; when it attempted to rise a certain loss of coordination was observed, and sometimes there were spasmodic contractions of the muscles (not fully typical of oxygen poisoning in that they were slower; these phenomena progressed rapidly. After decompression the condition remained practically unchanged. The rabbit lay on its side, groaned, and died 4—5 min after termination of decompression.

An increased carbon dioxide content when the oxygen content in the gas mixture was raised to 40% (11 experiments) apparently does not prevent the development of hyperthermia after DNP administration. In this series of experiments, most of the rabbits used had already been given DNP once or twice and had already been under increased or decreased oxygen pressure. In these animals, under the influence of a mixture of 20% carbon dioxide and 40% oxygen, the temperature either decreased 1.0° or showed a very slight increase (0.5°) after DNP administration. In rabbits which had not been subjected previously to any procedures, the rectal temperature during their stay in the chamber sometimes increased more than in the controls. For example, in experiment No. 32 (exposure 40 min) the increase in rectal temperature was 1.4° after switching over to breathing air. Death occurred after 35 min, during which time an additional temperature elevation of 1.5° was observed; the total increase in body temperature was 2.9°.

For eight out of nine rabbits a gas mixture of 20% carbon dioxide and 40% oxygen resulted in death either during the period of its use, or shortly after.

Of two control rabbits kept in this gas mixture for 40 min, one showed a decrease in body temperature by 1.7°; the other, which had first been given a sodium bicarbonate solution, 0.4°. Both remained alive.

In the case of rabbits subjected to pulmonary hyperventilation with air, the temperature increase resulting from DNP administration was somewhat less than under ordinary conditions. However, hyperventilation itself, as control experiments showed, leads to a considerable cooling of

the body. A comparison of the corresponding data shows that at the end of experiments with hyperventilation the difference between the temperatures of the control rabbits and those which had received DNP was much greater than the increment of temperature from DNP without hyperventilation. Hence, it follows that hyperventilation increases the hyperthermic effect of DNP.

Of five rabbits which had been given DNP, four died during experiments with hyperventilation (the duration of hyperventilation was 1 hr). Of six control animals, one died from hyperventilation.

Discussion of Results

From the data presented it follows that the change in partial oxygen pressure exerts a most pronounced effect on the development of DNP-induced hyperthermia, apparently by acting as a distinctive trigger mechanism. This is indicated by the following facts.

Halving the partial oxygen pressure (altitude of 5,500 m) immediately after DNP administration excluded the possibility of development of DNP-induced hyperthermia. However, if there is even the slightest interval between the DNP injection and the rabbit's ascent, a certain increase in temperature or maintenance of it at the initial level is noted. After switching to a gas medium with normal oxygen content an active temperature increase occurs. Finally, the very marked hyperthermic effect observed under compressed oxygen also indicates that oxygen and its partial pressure in the ambient medium is of decisive importance for the development of DNP- induced hyperthermia.

It is significant that here we are dealing not so much with an increase in the hyperthermic effect (total increase in body temperature during the experiment was almost the same as in the control) as with the very marked acceleration of this reaction — with the development of hyperthermia occurring in 5—10 min (instead of the 50—70 min in the control). Further increase in the temperature after decompression is less pronounced. and thereby the total increase in body temperature does not exceed the control figures

Data obtained concerning the effect of carbon dioxide on the development of DNP - induced hyperthermia is less distinct. Results of experiments with the effect of increased carbon dioxide content on animals which had received DNP on previous days do not permit drawing any conclusions about its role in the temperature changes noted. It is well known that very frequent DNP injections lessens the hyperthermic effect markedly, are tolerated with great difficulty by the animals, and even cause their death. Two experiments on rabbits being used for the first time indicate that increased carbon dioxide concentration does not inhibit the development of DNP- induced hyperthermia. However, it may be supposed that in these experiments a definite part was played by an increased oxygen content.

Hypocapnia, which evidently is also combined with a certain increase in the oxygen tension in the blood, increases the hyperthermic effect of DNP. This is expressed in a considerable elevation of body temperature, despite the pronounced cooling effect of hyperventilation itself.

The experiments showed that after DNP administration the rabbits have an altered tolerance to the effect of altered partial oxygen and carbon dioxide pressures. It might be concluded that this is explained by the simple summation of two unrelated unfavorable influences: the toxic effect of DNP, on the one hand, and the altered gas medium on the other. However, it seemed to us that there is a more deep- seated, intrinsic connection between these influences. It may be supposed, specifically, that a markedly increased oxygen requirement of the body after DNP administration causes the severe hypoxemic phenomena shown by the injected rabbits at a comparatively low altitude. Death of rabbits which had been given DNP and placed under compressed oxygen is possibly explained not by the increase in the toxic effect of oxygen as such, but by the marked increase in the action of DNP under these conditions and the excessive breakdown of macroergic compounds, with consequent active heat production.

In one way or another, the further workup of the problem of the action of DNP under conditions of altered partial oxygen and carbon dioxide pressures is of undoubted interest both to the study of the problem of conjugate respiration and phosphorylation, and of the mechanism of oxygen poisoning.

Conclusions

1. Change in the partial oxygen and carbon dioxide pressures in the inhaled air influences the development of 2—4 dinitrophenol- induced hyperthermia in rabbits.
2. Of greatest importance in the development of the hyperthermic effect after DNP injection is the partial oxygen pressure.
3. The reduction by half of the partial oxygen pressure in the inhaled air, which occurs during ascents to 5,500 m, prevents the development of hyperthermia.
4. Under an atmosphere of compressed oxygen a very marked acceleration of the course of the hyperthermic reaction to the DNP injection occurs.
5. The injection of DNP substantially changes the nature of the body's reactions to the effects of high and low partial oxygen and carbon dioxide pressures.

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THE EFFECT ON THE BODY OF A PROLONGED STAY IN A GAS MEDIUM WITH AN INCREASED CARBON DIOXIDE CONTENT

(Vliyanie na organizm dlitel'nogo prebyvaniya v gazovoi srede s povyshennym soderzhaniem uglekisloty)

While the effect on the bodies of animals of high carbon dioxide concentrations in the inhaled air has been studied quite thoroughly (Al'bitskii, 1911; Veselkin, 1913; Golodov, 1946; Zagryadskii, 1955; and others), this has not been the case with the effect of low carbon dioxide concentrations on the body. The comparatively narrow scope of studies made along this line (Berkovich and Shub, 1931; Brestkin et al., 1934; Gelhorn, 1948; Dejourus, 1958; Bernatskii, 1960) do not permit us to ascertain the possibility of animals or men remaining under these conditions for a long period or to characterize the aftereffect when the gas mixture is switched to that of ordinary atmospheric air.

The aim of the present work was to study the effect on the animal organism of breathing, for many hours, gas mixtures containing 3% and 5% carbon dioxide with normal oxygen content and with one of about 40%.

Method

The experiments were performed on 42 rabbits. The artificial gas medium was created in a pressure chamber having a volume of 0.37 cu.m, with a large window for observing the animal. The carbon dioxide content was checked with a GEUK-21 electric gas analyzer; that of the oxygen, with an "Oxytest" gas analyzer. The set carbon dioxide concentrations (3% and 5%) were maintained in the chamber by ventilating it whenever the carbon dioxide content became higher than a given figure. For the purpose of mixing the gases in the pressure chamber a fan was installed.

Before and after the effect of carbon dioxide on rabbits the frequency and depth of respiration, the ECG, EEG, and the rectal temperature were recorded, and a study was made of the blood (morphological composition and white blood count). For the purpose of recording the respiration, ECG, and EEG the rabbit was placed in a metal tray adapted to the shape of its body. While limiting body movement the tray permitted the animal to remain in a natural position and left its head free. Respiration was recorded on an oscillograph with a pressure cuff set on the animal. The ECG was made with a back-chest lead. Needles inserted under the skin

and held firm with a rubber bandage served as electrodes. The EEG was recorded by the G. T. Sakhiulina method (1953), with the use of a two-channel amplifier of the action currents and a two-beam cathode ray oscillograph. The electrodes were placed in the motor area of the cortex. In taking the EEG a study was also made of the reactivity of the brain to an audio stimulus. After the stimulus the functions being investigated were recorded every 15 min for 1.5—2 hrs. During the time the animals were in the chamber with increased carbon dioxide concentration, their respiratory movements were counted every hour, and their general behavior was observed.

The animals were exposed to the effects of 3% and 5% carbon dioxide for 6 and 12 hrs, with normal oxygen content and an oxygen content of about 40%. The air temperature in the chamber was kept between 18 and 20°.

In order to follow the dynamics of changes in the functions being investigated for a longer period than that occurring immediately after the stimulus, a number of experiments were performed outside the pressure chamber with the animals breathing the corresponding gas mixture through a mask. At the same time, a record was made of the respiration, ECG, and EEG, and the blood was analyzed.

The tracings of the respiration, ECG, and EEG were made in accordance with the above method.

Results of the Investigation

The behavior of the animals changed very slightly in a gas medium with an increased carbon dioxide content. Only for the first 1—1.5 hrs did the rabbits sit fixed in one place. Then they began to eat, to jump, wash themselves, sniff the walls of the chamber, and react in a lively manner to sound and light stimuli.

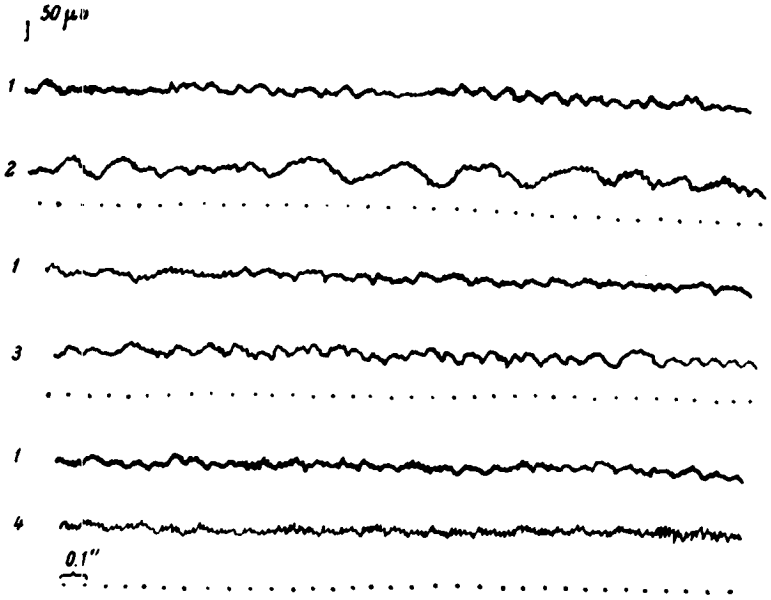
In the great majority of experiments (19 out of 22) an appreciable slowing of respiration was observed in the animals breathing an increased carbon dioxide and normal oxygen content.

Thus, in experiment No. 14 dated 13 July 1960 the rabbits' respiratory rate amounted normally to 220 per min; after an hour in the chamber with a 3% carbon dioxide content, 70 per min; after 12 hrs, 48 per min. With a carbon dioxide content of 5% in experiment No. 20 the respiratory rate after an hour of breathing the gas mixture was 112 instead of 212; after 12 hrs, 98 per min. On the average for all experiments, the maximum respiratory rate after an hour in an altered gas medium decreased by 68% from the initial figure; after 6 hrs, by 74%; after 12 hrs, by 78%. As a rule, the slowing of respiration was accompanied by a deepening of it and contraction of the accessory musculature to the respiratory rhythm. After the animal was removed from the chamber a marked increase in the respiratory rate was noted for 30—45 min.

The nature of change in the respiratory rate when the rabbits were in a gas medium containing 5% carbon dioxide and about 40% oxygen for 6—12 hrs was not much different from changes occurring with the gas medium containing 5% carbon dioxide only. As early as an hour after being in the altered gas medium a persistent slowing of respiration was observed (in 11 out of 13 experiments). After the animals were removed

from the chamber an increase in the respiratory rate was also observed in most experiments (in 9 out of 13). However, this increase in frequency was less pronounced than after breathing air containing 5% carbon dioxide. The increased respiratory rate was maintained usually for the first 15—30 min of the aftereffect period.

According to ECG data, the pulse rate of the rabbits in a gas medium with an increased carbon dioxide content and a normal oxygen content decreased considerably from the initial rate (25—35 per min) in the majority of experiments (in 17 out of 22). In five experiments an increase in the pulse rate by an average of 20—25 beats per min was observed. Studies of the ECG made every 15 min while the rabbit breathed a gas mixture with an increased carbon dioxide content showed a slowing of the heart rate as early as 15--20 min after switching to the gas mixture.



Changes in the rabbit's EEG after 10 hours in an atmosphere with an increased CO_2 content

1 —EEG in the air; 2 —EEG after a stay in a gaseous medium with a 5% CO_2 content; 3—the same with a 3% CO_2 content; 4 —the same with a 5% CO_2 and a 40% O_2 content. Dotted lines —time in 0.1 sec.

In a number of experiments the heart rate after the animal had been removed from the chamber did not reach the initial level after 45—60 min.

With a gas mixture containing an increased carbon dioxide content and an oxygen content of about 40%, immediately after the animals were taken out of the chamber such a characteristic slowing of the heart rate was not seen. Out of nine experiments a slowing of the heart rate was noted in three; in four there was an increase in the frequency, and in two experiments the pulse rate remained unchanged.

No specific features characterize changes in the various parameters of the ECG on breathing gas mixtures with increased carbon dioxide contents.

In a number of experiments an increase was noted in the voltage of the ECG waves, particularly T and R, and not uncommonly at the same time the T wave became more rounded. Often sinus arrhythmia was observed. After breathing a gas mixture containing 5% carbon dioxide and about 40% oxygen, a reduction in the voltages of the S and T waves and a very slight prolongation of the PQ interval were observed in addition to the changes indicated above. After 30—40 min of breathing atmospheric air the nature of the ECG was the same as initially.

In the case of breathing gas mixtures with 3—5% carbon dioxide and 21% oxygen a reduction of the rectal temperature was observed in the majority of experiments (17 out of 21); in two experiments there was an increase; in two the temperature remained unchanged. Reduction of the rectal temperature varied from 0.2—1.9°. In the two experiments where rectal temperature increased, the ambient temperature in the chamber was higher than usual and reached 26°.

With mixtures of 5% carbon dioxide and 40% oxygen there was a tendency toward an increase in the rectal temperature by 0.4—0.7° (in seven out of 12 experiments). On comparing electroencephalograms recorded in rabbits which breathed air with a 5% content of carbon dioxide and those which breathed a gas mixture of 5% carbon dioxide and 35—40% oxygen, essential differences were found in the nature of the electrical potential. Thus, in rabbits which breathed air containing 5% carbon dioxide, the normal rhythm, characterized by fast waves (35—45 per sec) and periodically-occurring slow waves of the α-wave type (12—16 per sec), changed markedly in the direction of absolute predominance of slow high-voltage potentials after the animal had been removed from the chamber. The EEG of this nature was maintained, as a rule, for 45—60 min. During this period the animals were completely immobile and did not react to sound stimuli. Most of them showed pronounced exophthalamus. The EEG of rabbits which breathed a mixture of oxygen and carbon dioxide was absolutely different. In the aftereffect period an increase was noted in the frequency and amplitude of β-potentials with an almost complete absence of slow waves. In these rabbits a high degree of motor activity was observed.

The segments of the EEG presented on the figure depict graphically these differences in the nature of bioelectrical activity of the cerebral cortex in both series of experiments.

The aftereffect period of rabbits exposed to the gas medium containing 3% carbon dioxide for 6 and 12 hrs was characterized by the appearance of slow high-voltage waves on the EEG. As a rule, this EEG was maintained for 45 min after the rabbit had been taken out of the chamber. Gradually areas with an increased β-rhythm were noted on the EEG. The animal regained its normal motor activity 60 to 90 min after it had been removed from the chamber. At the same time a progressively greater normalization of the EEG could be seen.

An atmosphere containing 5% carbon dioxide resulted in considerable increase in the white blood count during the aftereffect period. This increase 3,000—4,000 above the initial figure, was maintained for two days. The morphological picture was characterized, in contrast to the initial background, by increase in the pseudoeosinophil (segmented) count and a reduction of the lymphocyte count. When the carbon dioxide content was equal to 3%, similar changes were observed in the white blood. When, in

addition to carbon dioxide, there was an increased oxygen content in the ambient atmosphere, the rabbits showed a very slight leukocytosis only on the second day after the effect. In addition, a reduction in the pseudo-eosinophil count and an increase in the lymphocyte count occurred.

Discussion of Results

The experiments performed showed that after the animals had been for many hours in a gas medium with a 3% or particularly a 5% content of carbon dioxide content, pronounced functional changes were observed in respiration, the cardiovascular system, and central nervous system. This is in agreement with data obtained by other authors.

M. P. Brestkin (1934), studying problems involved in assuring physiological conditions for the crew in a stratosphere balloon gondola, showed that increase in the carbon dioxide concentration of the air to 3% failed to produce any pronounced abnormalities in the body. Thus, only a moderate increase in the rate and depth of respiratory movements was observed. With increase in the carbon dioxide concentration to 6% the subject became incapable of working. The author believes that to maintain a person's efficiency in the gondola it is advisable to keep the carbon dioxide concentration at a level of 0.5—1%.

Simons and Archibald (1958), on the basis of experience accumulated as a result of investigations in the submarine fleet, point out that when human beings are in an airtight cabin for a prolonged period, the permissible limit for the carbon dioxide concentration is 3%. However, the authors believe that to prevent reduction in efficiency it would be more "cautious" to use a 1% carbon dioxide concentration.

Our experiments showed that essential functional changes occurred in animals in an airtight chamber for 6—12 hours when the carbon dioxide content was 3% and 5%. These changes were expressed in a slowing and deepening of respiration, a slowing of cardiac activity, increase in the voltage of the ECG, and lowering of the body temperature.

With a rapid switch to atmospheric air a pronounced aftereffect was observed. It was expressed in marked inhibition of motor activity, increase in the respiratory rate, very slight slowing of the heart rate, and leukocytosis. The degree of these functional changes is dependent not only on the concentration of carbon dioxide and the duration of its effect, but also on the individual characteristics of the body. Most characteristic of the carbon dioxide aftereffects were signs of marked inhibition of the central nervous system, expressed in an absolute predominance of slow high-voltage potentials on the EEG as well as the animal's lack of reaction to audio stimuli. As is well known, V. N. Bernatskii (1960) found signs of prolonged transmarginal inhibition in rabbits during an investigation of conditioned reflexes and in the EEG after they had breathed a gas mixture containing 6--7% carbon dioxide for 1.5 hrs. In our experiments signs of inhibition were found even after breathing air containing 3% carbon dioxide.

It should be emphasized that animals in an airtight chamber containing 3—5% carbon dioxide for a long time, show signs of adaptation to an increased carbon dioxide content. After being in the gas medium for 1—2 hrs

the respiration of the animals became even; they reacted in a lively manner to light and sound stimuli, ate, etc. However, when there was a change in the gas composition (i.e., a switch to breathing ordinary atmcspheric air) pronounced functional changes were again observed, and deep inhibition of the central nervous system developed. Probably, the physiological mechanisms which provide for adaptation to increased carbon dioxide concentrations lose their beneficial significance when there is a marked change in the composition of the gas medium. In this connection, the question arises as to the significance of a gradual change from an altered gas medium to the usual atmospheric conditions and as to the optimum duration of the change, particularly after many days of being in a gas medium with an increased carbon dioxide content. This problem requires experimental study.

In experiments with a prolonged stay under a gas medium containing 5% carbon dioxide and about 40% oxygen, the aftereffects after switching to atmospheric air were found to be less pronounced. The aftereffect period in these experiments was shorter, inhibition of the central nervous system was less prolonged, and a slight increase in the respiratory rate was observed. Therefore, the addition of about 40% oxygen to the gas medium containing an increased carbon dioxide concentration reduces the unfavorable effect of carbon dioxide and makes it easier for the organism to switch over to normal atmospheric air. This is evidently a result of the antagonism between the effects of oxygen and carbon dioxide in their action on the body, which has been pointed out by P. M. Al'bitskii (1911), E. Gelhorn (1948), and a number of other authors.

I. I. Golodov (1946) determined the fact that the increased oxygen content of the gas mixture lessens the anesthetic effect of high carbon dioxide concentrations. Our data permits us to suppose that increased oxygen concentrations (as high as 40%) considerably reduce the unfavorable effect of prolonged breathing of gas mixtures containing carbon dioxide. This fact may be of practical importance in cases where a change is made from altered gas conditions to ordinary atmospheric air.

Conclusions

1. A gas medium containing 3—5% carbon dioxide acting on rabbits for 6—12 hrs causes functional changes in respiration, cardiac activity and heat regulation.

2. A rapid switch of the animals from a medium with an increased content of carbon dioxide to ordinary atmospheric air is accomplished by a marked aftereffect lasting 1.5—2 hrs.

3. The most characteristic manifestation of the aftereffect of prolonged breathing of gas mixtures containing an increased carbon dioxide content is deep inhibition developing in the central higher nervous system centers of the rabbits.

4. The aftereffect period is considerably reduced (to 30 min) and is accompanied by less pronounced functional changes when the 5% carbon dioxide content is mixed with 35—40% oxygen.

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B. A. Nessirio

ADAPTIVE REACTION OF THE HUMAN BODY TO THE REPEATED EFFECTS OF INCREASED AIR PRESSURE (ACCORDING TO DATA ON THE STUDY OF HIGHER NERVOUS ACTIVITY)

(Prisposobitel'naya reaktsiya organizma cheloveka k povtornomu deistviyu povyshennykh davlenii vozdushnoi sredy (po dannym izucheniya vysshei nervnoi deyatel'nosti))

As experience in diving practice has shown, if a person is repeatedly under pressure, the output of work done under these conditions increases. However, no special, regular studies of adaptive reactions of the human or animal organism to repeated effects of increased air pressures can be found in the available literature. Concerning the overall physiological effect of compressed air on animals and man, it has been shown that the anesthetic properties of increased nitrogen pressures are of prime importance (Behnke et al., 1935, 1938; N. V. Lazarev, 1941; L. A. Orbeli, et al., 1944; G. L. Zal'tsman, 1961; and others).

The object of the present work was to study adaptive reactions of the human body to the repeated effects of increased air pressures.

Method

The investigations were made on seven divers between the ages of 19 and 30 with approximately the same length of diving experience. Each subject was repeatedly exposed to the effect of the same constant pressure of 4, 6 and 8 atm in a dry pressure chamber. In order to evaluate the adaptive reaction, the higher nervous activity of the subjects was studied.

Under normal pressure in the chamber, the conditioned motor reflexes were elaborated on an electric reflexometer by the following means: speech reinforcement to a painful cutaneous stimulation with a current, a steady and a flickering white light with a frequency of 120 per min (C_{120}), and a differential flicker frequency of 100 per min, as well as verbal designations of the direct stimuli. To evaluate the condition of internal inhibition a delayed conditioned reflex to red light with a lag of 6 or 10 sec was elaborated. The verbal reactions were studied by means of the verbal sterotype method which we modified: to each of three verbal stimuli ("table", "chair", "rap") written on separate glass plates and shown in an arbitrary order, the subject was to respond with a single word, respectively, "old", "new", and "weak". To one of these word stimuli (different

in each investigation) there was to be no response. Mental efficiency was studied by means of arithmetic exercises (the addition of 2 digit numbers).

The stimuli of the positive conditioned motor reflexes were used serially 5—7 times with pauses of 10—20 sec between them, while differentiation and the verbal stimuli of the verbal stereotype were used 3—4 times each. The sequence of stimuli to motor reactions was constant in each determination; the sequence of verbal stimuli varied. A record was made of the latent periods of the reactions (with an accuracy within 0.01 sec) and the magnitudes of the conditioned motor reflexes (in relative units on a scale of 100 divisions). All the studies took 15—18 min; they were made at normal air pressure immediately before the beginning of descent and then were repeated immediately after completion of compression. The interval between the repeated descent was usually 1—3 days.

To check the results obtained, an additional investigation was made of 19 untrained student divers. Higher nervous activity was studied by means of a proofreading method according to standard tables of V. Ya. Anfimov and A. G. Ivanov- Smolenskii.

The indices of higher nervous activity changes occurring under conditions of increased pressre were treated statistically by the method of "evaluation of the differences between the means, in the case of related data" (Kaminskii, 1959). The "closeness of connection" between the variations of these indices in the case of repeated applications of pressure and the number of "descents" was determined by the correlation method. A correlation coefficient above 0.3 constituted an indication of a positive connection; such a connection was regarded as an expression of the biological adaptive reaction of the organism.

Results

In the case of pressures over 4 atm, the subject developed the following subjective sensations: numbness of the lips and tongue, dull pain in the skin, seeing "sparks flickering before the eyes"; two subjects noted auditory hallucinations, nausea and desire to vomit. During the course of 27—29 repeated applications of pressure the subjective signs of nitrogen intoxication did not decrease appreciably. At the same time, however, the subjects noted that during repeated descents they gradually felt less on guard and less anxious — feelings associated with the appearance of unusual subjective sensations — and that there was an increase in the sense of work in the power of analyzing one's own actions and restraining emotional reactions.

With the change in the feeling of well- being during the stay under pressure, a simultaneous increase in the latent period and the magnitude of the conditioned reflexes was noted. Thus, under a pressure of 6 atm the latent period of the reaction to painful cutaneous stimulation with a current increased by an average of 0.05 sec (21%); of the reaction to white light, by 0.04 sec (9.7%); to C_{120}, by 0.18 sec (4.8%). The time lag increased by 1.14 sec (18.7%); the latent period of verbal reactions increased by 0.11 sec (8.2%); and, finally, the time needed for solving the arithmetic problems increased by 0.23 sec (7.7%). The probability

TABLE 1

Number of repeated descents necessary for relative stabilization of the indices of conditioned reflex activity

Subjects	Air pressure (in atm)	Indices of higher nervous activity															
		Motor reaction to stimulation with a current		Motor reaction to white light		Delayed conditioned reflex to red light		Motor reaction to M_{120}			Differentiation to M_{120}	Verbal designations of the direct stimuli		Verbal stereotype		Calculations	
		latent period	magnitude of the reactions	latent period	magnitude of the reactions	latent period	magnitude of the reactions	latent period	magnitude of the reactions	frequency of omissions	frequency of omissions	latent period	magnitude of the reactions	latent period	Number of errors	latent period	number of errors
Zh-v	4	6	—	3	4	—	4			—				2	1	4	2
S-v				2	3	—	—	—	—	—	—			—	—		
R-v				—	—	—	—	—	4	—	—	4	—				
B-ko	6			3	3	—	—	2	—	—	—	1	3				
Zh-i		—	3	3	3	—	7	1	3	—	—	—	2	2	—	—	
N-i				4	—	—	—	—	3	—	—			—	—		
K-i		3	—	—	—	—	—	2	—	—	4	—	2	—	—	—	—
B-ko		—	2	—	—	—	—	—	1	—	9	4	—	3	—	—	—
V—v	8	—	3	—	5	—	—	5	—	—	—	—	—	—	—	—	—
B-sh		2	—	—	—	—	2	—	1	—	—	2	—	—	—	—	—
P-lo	10			6	3	—	4	—	3	—	—	7	2				

Note. The dash indicates that no relative stabilization of the indices occurred.

that these changes were significant was 80—99%. The magnitude of the conditioned motor reflexes increased by an average of 2.5—6.2 units (6.7—15.2%) with a probability of 95—99%.

With the use of the inhibitory stimulus (C_{100}) under pressure, breakdowns of differentiations were noted, and in only one subject was there more frequent inhibition of the positive reaction to C_{120}. The number of errors made in solving arithmetic problems increased. As a rule, no qualitative disorders were observed in the study of the verbal stereotype. All the subjects did their proofreading work more slowly (on the average, by 10.8%); many omitted positive symbols or even whole lines. The ability to differentiate the symbols was maintained.

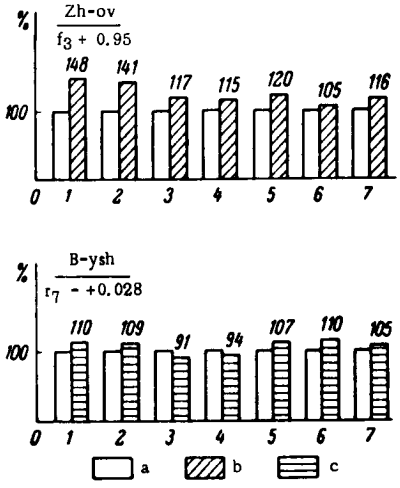
TABLE 2

Number of repeated descents necessary for normalization of indices of proofreading tests

Subject	Air pressure (in atmospheres)	Number of correctly underlined symbols (rate of work)	Number of positive symbols missed	Number of incorrectly underlined symbols	Number of entire lines omitted
K-n	4	—	—	—	—
E-o	4	—	—	—	—
S-ko	4	—	—	—	—
K-k	4	—	2	—	2
S-a	4	2	2	—	—
K-v	4	—	—	—	—
N-k	4	—	—	—	—
Ch-i	4	—	—	—	—
V-v	4	—	—	—	—
M-i	4	—	—	—	—
K-ya	6	7	—	—	—
Z-ka	6	6	—	—	—
A-v	6	7—11	—	—	—
Zh-v	6	3	—	—	—
K-o	6	4	—	—	—
G-v	6	3	3	—	—
I-o	6	5	—	—	—
Sh-k	6	2	2	—	2
L-n	6	—	—	—	—

Note. The dash indicates that no relative normalization of the indices occurred.

All these changes were directly related to the degrees of pressure used, to the individual sensitivity of the divers, to the effect of nitrogen and to the difficulty of the tasks.



Dynamics of changes in the latent periods of the verbal reaction in divers Zh-v and B-ysh (average figures)

a — air pressure of 0 atm; b — 4 atm; c — 8 atm. On the abscissa, the ordinal numbers of the tests; on the ordinate, the latent period

The figure shows results of determinations of the latent periods of verbal reactions with the use of repeated effects of compressed air in two subjects, who differed in their individual sensitivities to the nitrogen effect. In one of them (Zh-va), after a pronounced increase in the latent period at the time of the first determination under an air pressure of 4 atm, a distinct reduction occurred in the third determination (the correlation coefficient r for the first three descents was 0.95). In subsequent determinations stabilization of the latent period was noted. In another subject (B-sha) under an air pressure of 8 atm the latent period of the verbal reactions in the first determination exceeded the initial figures by a total of 10% and in subsequent determinations it remained at approximately the same level (r=+0.028).

Therefore, in the first case it was possible, from the change in the latent period of verbal reactions, to note adaptation to the repeated nitrogen effect of the compressed air after three descents; in the last subject no pronounced adaptation occurred.

The results of the other studies made, treated in a similar way, are shown in Table 1.

From the data obtained it follows that in the determination of the latent period and the magnitude of the conditioned reactions an adaptive reaction could be found in about half the cases* The rate of relative normalization of the latent periods of the conditioned motor reactions (to the painful cutaneous stimulation with the current and to white light) and the verbal reactions (verbal stereotype) was approximately the same; accustomation occurred during the first three to seven descents in the majority of cases.

* In most cases it was impossible to determine definitely the trends of the variation in the erroneous respones, because they were so few.

Similar results were obtained in the study of the adaptive reaction of 19 student divers by the simplified method — by means of proofreading tests (Table 2). If we judge by the increase in the rate of work, adaptation of the subject also occurred during the first two to seven descents in the majority of cases.

The studies showed that the rate of adaptation of the subjects to the action of compressed air depended on their individual sensitivities to nitrogen, the degree of pressure used, and the difficulty of the task. Under conditions otherwise equal, the greater these three factors, the greater the number of descents necessary for relative normalization of higher nervous activity.

In conclusion, we should dwell on the results of special control studies made to determine the effect of various factors in the experimental situation on the subjects' conditions. It was found that no definitely directed changes in higher nervous activity resulted from such associated factors as increased air temperature, noise of incoming air, increased partial oxygen and carbon dioxide pressures, and mechanical effects of gas pressures equivalent to those acting on the human body when air pressure is raised to 4—10 atm. This suggests a connection between the dynamics of changes in conditioned-reflex activity found in the subjects during repeated tests under pressure, and accustomation to the nitrogen effect in the compressed air.

Discussion of Results

The investigations made showed that the adaptive reaction occurring from repeated applications of pressure is not universal. During the first seven descents an appreciable recovery of the simplest, chiefly quantitative indices of higher nervous activity was noted, such as those of latent period, magnitude of the reaction, as well as behavioral reactions.

Recovery of these functions may, apparently be regarded as the result of gradual weakening of the toxic effect of nitrogen on the higher central nervous system centers. Concerning the mechanism of action of increased nitrogen pressures, first should be mentioned a disorder of processes of internal inhibition (disruption of differentiation, delay, etc.), which was shown in special studies of G. L. Zal'tsman (1961) and confirmed by our data. Therefore, the object of training the human body to the initial anesthetic effect of nitrogen is, in our opinion, to normalize processes of internal inhibition and reduce the generalized inhibition of cortical reactions. The data obtained permits us to suppose that recovery of various types of internal inhibition does not occur uniformly but depends on different factors, primarily on the complexity of the task being carried out. Thus, comparatively simple tasks (negative responses to word stimuli in a verbal stereotype, differentiation of letters, combinations of them in proofreading) were carried out almost without error even the first time the subjects were under pressure.

Emotional, behavioral and specially elaborated motor reactions were appreciably disinhibited in the first and second tests, but during the course of repeated nitrogen effects, became progressively more adequate. Therefore, special training was needed for relative normalization of these functions.

The more difficult task of differentiating between C_{100} and C_{120} frequencies was frequently performed incorrectly, not only during the first descent but also in subsequent ones, i.e., despite training. Only a few subjects showed a tendency toward gradual improvement.

Finally, in the investigation of the delayed conditioned reflex it was impossible to observe even a tendency toward normalization of the latent period, despite its distinct increase in the first and repeated descents.

From a practical aspect, the results obtained indicate that such training sessions for divers can bring about a certain reduction of the paralyzing effect of the anesthetic properties of nitrogen on the functions of the higher nervous system centers. Thereby it is possible to increase the rate at which mental and physical work is performed under increased pressure, to adequately adapt the divers to evaluating their own feeling of well-being and the surrounding situation. The latter may be of definite importance in increasing the safety of deepwater dives.

Conclusions

1. A study was made of the dynamics of higher nervous activity indices of subjects repeatedly under conditions of increased air pressures (4—8 atm). The reaction demonstrated has the nature of an adaptive reaction.

Relative normalization of the indices of higher nervous activity occurs in the majority of cases after three to seven descents.

2. The nature of the adaptive reactions depended on the degree of disorder of higher nervous activity under pressure. The greater the pressure, the more sensitive the subject to the anesthetic effect of nitrogen, and the more difficult the task, the more pronounced were the changes in higher nervous activity and the greater were the number of repeated descents necessary for relative normalization of them.

3. Training sessions against the initial anesthetic effect of nitrogen in divers permit an increase in the output of their work under increased pressure.

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Yu. M. Polumiskov

THE PROBLEM OF THE MECHANISM OF OCCURRENCE OF PULMONARY PRESSURE TRAUMA DURING THE BREATHING OF AIR AND OXYGEN

(K voprosu o mekhanizme vozniknoveniya barotravmy legkikh pri dykhanii vozdukhom i kislorodom)

A small number of papers (Polak and Adams, 1932; German and Alekseev, 1955; and others) have been written on the study of the etiology and pathogenesis of pressure trauma of the lungs.

To date, the effect of the degree, rapidity of increase, and duration of intrapulmonary pressure on the occurrence of pulmonary pressure trauma remains unclear. No investigation has been made of the effect of repeated increases of intrapulmonary pressure on the course of pressure trauma.

Our investigation was on these problems.

Method

The experiments were performed on cats of both sexes weighing from 2—5 kg, under evipan anesthesia. To prevent blood coagulation, a solution of germanine (0.2 g/kg body weight) or heparin (200—300 IU/kg) was given intravenously before beginning the experiment. During the course of the experiment the blood pressure, respiration, intrapleural pressure, intrapulmonary pressure and time marking were recorded on a kymograph.

In recording the respiration, an inflatable rubber cuff with soft ties which did not prevent chest expansion was set on the chest and upper abdomen. Intrapulmonary pressure was measured by introducing into the intrapleural space of the right or both lungs large-calibre needles connected to a mercurial or water manometer and having a side process for removal of the excess gas from the intrapleural space (suction of gas).

The animal was tracheotomized, and to one end of the T-piece of the tracheotomy cannula a rubber tube was connected for the purpose of increasing the intrapulmonary pressure. The gas mixture was fed through a regulator, which assured the necessary speed in increasing intrapulmonary pressure and the requisite duration of its action.

The experimental animals were given air or oxygen to breathe.

Gas emboli penetrating into the blood stream in the case of pulmonary pressure trauma were caught by means of a glass cannula trap 2 ml in volume which had first been filled with germanine solution (0.2 g) or

heparin solution (200 IU). The cannula traps were set in the left common carotid artery and right femoral artery. A description of them is given in the article by P.M. Gramenitskii and A.A. Savich, published in this collection.

Results of the Experiments

Pneumothorax was determined by the occurrence of positive intrapleural pressure and the results of subsequent autopsy of the animals.



The effect of an increase in intrapulmonary pressure on the change in blood pressure, respiration, and intrapleural pressure from pulmonary pressure trauma. Kymogram of experiment No. 14, dated 20 April 1960

From right to left, reading upward: Time marking — 5-second intervals; hand-switched marking of the rate of increase and duration of the effect of intrapulmonary pressure; intrapulmonary pressure (in mm Hg); intrapleural pressure on the right side of the chest (in mm H_2O); blood pressure (in mm Hg); respiration.

To produce pulmonary pressure trauma, the degree of intrapulmonary pressure was increased gradually from 5 to 60 mm Hg.

If with increase of intrapulmonary pressure to 5—10 mm Hg no change occurred in the intrapleural pressure indicating pneumothorax, after 5—7 min it was raised to 20 mm and then by 10—15 mm each time until the intrapleural pressure became positive, indicating that pneumothorax had occurred.

The kymograph in experiment No. 14 gives an idea of the nature of the changes occurring in pressure trauma of the lungs.

In experiment No. 14, before the beginning of the procedure, the blood pressure amounted to 105 mm; the pulse was 72 per min; respiration was deep, its rate 24 per min. The intrapleural pressure on the right side of the chest was equal to 20 mm of water. Over a period of 30 sec the intrapulmonary pressure rose to 34 mm, at which level it was maintained for 40 sec. Thereby the blood pressure dropped to 16 mm; the pulse, to 228 per min; apnea occurred. In the 35th second of the effect of greatest

intrapulmonary pressure the intrapleural pressure was equal to 52 mm of water. The intrapulmonary pressure dropped to atmospheric in one second. Ten seconds later the blood pressure was 145 mm; the pulse, 144; there was apnea; the intrapleural pressure was equal to 50 ml of water. The first inspiration occurred after 30 sec.

The clinical picture 120 sec after reduction of intrapulmonary pressure was as follows: blood pressure 110 mm Hg; pulse, 108; respiration deep, its rate 28 per min; intrapleural pressure, 50 ml of water.

TABLE 1

The occurrence of pulmonary pressure trauma (in numbers of cases)

Kind of animal	Total number of experiments	Degree of intrapulmonary pressure (in mm Hg) at which pulmonary pressure trauma occurs				
		10-20	21-30	31-40	41-50	51-60
Cats	46	11	11	13	10	1
Dogs	2	—	—	1	—	1
Total . .	48	11	11	14	10	2

The cat was killed 20 min after the reduction of intrapulmonary pressure to atmospheric. At autopsy emphysema of both lungs was found; there was a large number of punctate and focal hemorrhages on the costal surface and at the lung roots. No other changes were found.

For the purpose of determining the intrapulmonary pressure at which pulmonary pressure trauma occurs, 46 experiments were performed on cats and two on dogs; the data obtained is shown in Table 1.

Pneumothorax in pressure trauma first occurred on one side, as a rule. Further increase in the intrapulmonary pressure or increase in duration at the same pressure leads to pneumothorax on the other side also.

Of the 48 experiments presented, pulmonary pressure trauma occurred in 10 when the animal breathed oxygen. In these cases pneumothorax occurred at the same degrees of intrapulmonary pressure as when cats breathe air.

At autopsy emphysema of both lungs and a large number of punctate and (in some experiments) focal hemorrhages were found in all animals. Gas bubbles were found around the blood vessels of the lung roots, sometimes in the mediastinal tissues.

All the experiments of this series showed that at a pressure of less than 60 mm Hg pulmonary pressure trauma was never accompanied by arterial gas embolism.

TABLE 2

The occurrence of arterial gas embolism in pulmonary pressure trauma (number of cases)

Degree of intrapulmonary pressure (in mm Hg)	Number of experiments	Pulmonary pressure trauma without arterial gas embolism		Pulmonary pressure trauma with arterial gas embolism	
		Cats	Dogs	Cats	Dogs
60-100	27	18	—	9	—
101-140	39	20	1	17	1
141-200	8	4	1	3	—
Total	74	42	2	29	1

TABLE 3

Pulmonary pressure trauma as a function of rapidity of increase of the intrapulmonary pressure (number of cases)

Intrapulmonary pressure (in mm Hg)	Number of experiments	Duration of increase of intrapulmonary pressure (in sec)	
		1-5	10-30
10—30	22	6	16
31—60	26	13	13
Total	48	19	29

TABLE 4

Arterial gas embolism in pulmonary pressure trauma as a function of rapidity of increase in the intrapulmonary pressure from 60 to 100 mm Hg (number of cases)

Nature of expression of pulmonary pressure trauma	Number of experiments	Duration of increase in intrapulmonary pressure (in sec)	
		1-5	10-30
Without arterial gas embolism	44	19	25
With arterial gas embolism	30	13	17
Total	74	32	42

Subsequently, 71 experiments were performed on cats and three on dogs to determine the degree of intrapulmonary pressure at which pressure trauma of the lungs is accompanied by gas embolism of the blood vessels. The results obtained are shown in Table 2.

From Table 2 it is evident that with increase in the intrapulmonary pressure from 60 to 200 mm Hg, pulmonary pressure trauma with arterial gas embolism occurred in 30 out of 74 experiments (40.5%), i.e., pulmonary pressure trauma was observed more often unaccompanied by gas embolism. Increase in the intrapulmonary pressure above 140 mm Hg does not result in the more frequent occurrence of arterial gas embolism. We believe that arterial gas embolism occurs in an animal when the appropriate anatomical and physiological conditions are created for gas entering the arterial blood stream. In other cases it enters the mediastinal tissue, tissue of the retroperitoneal space, and subcutaneous tissue of the upper portion of the chest and neck. In most experiments further increase in pressure only increases the gas entering these areas.

A comparison of the results obtained from the breathing of air and of oxygen shows that the nature of the gas mixture has no essential influence on the occurrence of arterial gas embolism in pulmonary pressure trauma. Thus, with breathing of air, embolism of the blood vessels was observed in 25 out of 60 animals (41.7%); with oxygen, in 5 out of 14 (35.7%).

Autopsy on the animals showed that increase in the intrapulmonary pressure leads to a great accumulation of gas in the mediastinal tissue, tissue of the retroperitoneal space, neck, and chest. In the case of pulmonary pressure trauma with arterial gas embolism, in cats a considerable number of gas bubbles was found in the medium-sized and small arteries.

An interesting characteristic was observed: in animals with pulmonary pressure trauma and arterial gas embolism, considerably more air accumulated in the tissue of the anterior mediastinum and neck; in animals without gas embolism under the influence of the same degrees of intrapulmonary pressure, the gas more frequently went into the tissue of the posterior mediastinum and retroperitoneal space. This fact confirms our opinion that in pulmonary pressure trauma, aside from the degree of intrapulmonary pressure, a great part is played by anatomic characteristics, which have an influence on the direction of movement of the gas in the body.

A study of the effect of rapidity of increase of intrapulmonary pressure on pressure trauma of the lungs showed that with extension of the period of such increase, pulmonary pressure trauma tended to occur at lower pressures (Table 3).

As is evident from Table 4, in these experiments the effect of the rapidity of pressure increase on the occurrence of gas embolism is manifest.

Tables 5 and 6 show the results of experiments on the occurrence of pulmonary pressure trauma and accompanying gas embolism as a function of the duration of action of maximum intrapulmonary pressure.

As is evident from Table 5, the longer the period of action of the maximum intrapulmonary pressure the more frequently pneumothorax occurs at a lower pressure.

As is evident from Table 6, increase in the period of action of the maximum intrapulmonary pressure leads to the more frequent occurrence of pulmonary pressure trauma accompanied by arterial gas embolism.

TABLE 5

Pulmonary pressure trauma as a function of the duration of action of intrapulmonary pressure (number of cases)

Intrapulmonary pressure (in mm Hg)	Number of experiments	Duration of action of intrapulmonary pressure (in sec)		
		1-20	21-40	41-60
10-40	36	11	18	7
41-60	12	6	5	1
Total	48	17	23	8

TABLE 6

Arterial gas embolism in pulmonary pressure trauma as a function of the duration of action of intrapulmonary pressure, from 60 to 200 mm Hg (number of cases)

Nature of expression of pulmonary pressure trauma	Number of experiments	Duration of action of intrapulmonary pressure (in sec)		
		1-20	21-40	41-60
Without arterial gas embolism	44	22	15	7
With arterial gas embolism	30	13	11	6
Total	74	35	26	13

To determine the effect of a repeated increase in the intrapulmonary pressure on the occurrence of arterial gas embolism in pulmonary pressure trauma, we performed experiments on 57 animals with induced pulmonary pressure trauma in which the intrapulmonary pressure was increased from 2 to 6 times in each experiment. In all, in 57 experiments the pressure was increased repeatedly 207 times. In 148 cases the intrapulmonary pressure was increased from 10 to 60 mm Hg; in 59 cases, from 61 to 200 mm Hg. Of this number (59) the pressure in 20 experiments was raised again in animals with pulmonary pressure trauma accompanied by arterial gas embolism.

Out of all 207 cases, gas bubbles reappeared in the cannula traps when the intrapulmonary pressure of 80—120 mm Hg was reached in only 2 animals. When the pressure was raised a second time arterial gas embolism occurred in one cat which had previously had gas embolism; in another cat it occurred for the first time.

The second pressure rise always led to the entrance of additional gas into the intrapleural space, the mediastinal tissue, retroperitoneal space,

neck, and chest, causing a deterioration of the course of pulmonary pressure trauma.

Discussion of Results

The experiments performed showed that pneumothorax in dogs and cats always occurs when the intrapulmonary pressure is raised from 10 to 60 mm Hg.

We determined the occurrence of pulmonary pressure trauma by the appearance of positive intrapleural pressure and by results of autopsy. The possibility cannot be denied that pneumothorax occurs without injury to the visceral pleura or change in the intrapleural pressure when the gas can enter the interstitial spaces of the lung roots. Nevertheless, the data obtained in our experiments permitted us, with a certain degree of reliability, to make dynamic observations of the changes occurring as a result of pulmonary pressure trauma.

Arterial gas embolism accompanying pulmonary pressure trauma occurred in our experiments only with increase in the intrapulmonary pressure from 60 to 200 mm Hg (in 30 out of 74 experiments).

It should be noted that the occurrence of arterial gas embolism in pulmonary pressure trauma in the cat or dog was judged by the appearance of visible gas bubbles in the cannula traps and, at autopsy, in small and medium- sized arteries of the leaft heart.

There is the possibility that in pulmonary pressure trauma invisible gas bubbles may form and penetrate into the blood stream, but our method did not permit such a determination.

On the basis of data obtained in these experiments it may be supposed that a determinative factor in the occurrence of pneumothorax in cats and dogs with pressure trauma is the physiological limit of resistance of lung tissue to the intrapulmonary pressure created. This resistance differs in each animal but is equal to no more than 55—60 mm Hg.

The increased duration of the effect of intrapulmonary pressure reduces the capacity of the lung tissue for withstanding the pressure created, and pulmonary pressure trauma occurs at a lower pressure.

It cannot yet definitely be explained why at a pressure above 60 mm Hg arterial gas embolism accompanies pulmonary pressure trauma in some cases and not in others. It may only be supposed that the occurrence of arterial gas embolism in pressure trauma depends on some anatomic or physiological conditions which are responsible for gas entering into the blood stream or mediastinal tissue, tissue of the retroperitoneal space, the neck and chest when the pressure exceeds 60 mm Hg. Thus, gas embolism occurred most often when the intrapulmonary pressure was between 60 and 130 mm Hg while subsequent increase in the pressure rarely produced it. Increase in the duration of action of intrapulmonary pressure leads to the more frequent occurrence of gas embolism, but only up to a certain limit.

Conclusions

1. Pneumothorax occurs in dogs and cats when the intrapulmonary pressure is increased from 10 to 60 mm Hg, most often between 20 and 40 mm Hg.

2. Increase in the duration of action of intrapulmonary pressure causes pressure trauma of the lungs at lower pressures.

3. In some cases of pulmonary pressure trauma visible arterial gas embolism can occur when the intrapulmonary pressure is raised above 60 mm Hg and is accompanied by the simultaneous entrance of a large number of gas bubbles into the left heart and the arteries of the entire body of the animal.

4. The nature of the gas mixture breathed is of no essential importance in the mechanism of occurrence of pulmonary pressure trauma or accompanying arterial gas embolism.

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THE PROBLEM OF THE EFFECT OF BREATHING OXYGEN IN THE RESORPTION OF GAS EMBOLI IN THE VASCULAR SYSTEM OF AN ANIMAL AND ON THE COURSE OF PULMONARY PRESSURE TRAUMA

(K voprosu o vliyanii dykhaniya kislorodom na rassasyvaemost' gazovykh embolov v krovenosnoi sisteme zhivotnogo i techenie barotravmy legkikh)

According to available bibliographic sources on animal experiments, the significance of breathing oxygen in pulmonary pressure trauma with arterial gas embolism has not been studied to date. However, the works of P. Ber (1878), B. D. Kravchinskii and S. P. Shistovskii (1936), V. A. Alekseev (1945), A. P. Brestkin (1952), and others have proved that the use of oxygen is very effective in accelerating the resorption of nitrogen by the body, and in prevention and treatment of decompression sickness.

With the aim of determining the effect of breathing oxygen on resorption of gas bubbles in the blood vessels with pulmonary pressure trauma, we performed 17 experiments on cats.

Method

The method of performing these experiments has been described, by and large, in our articles, "The Problem of the Mechanism of Occurrence of Pulmonary Pressure Trauma During the Breathing of Air and Oxygen" and "The Problem of Treatment of Pulmonary Pressure Trauma", published in this collection.

In five experiments, animals were switched to breathing oxygen 30—50 min before beginning the increase in intrapulmonary pressure. Then pulmonary pressure trauma was produced, accompanied by arterial gas embolism. Where necessary, gas was aspirated from the pleural cavities of the animal. After recovery of respiration and circulation the cat continued to breathe oxygen. The degree of reduction of gas bubbles in the blood stream was determined by the change in their number in the cannula trap of the left carotid artery. At the end of the experiment the animal was killed, and an autopsy was performed.

In five experiments pulmonary pressure trauma with arterial gas embolism was produced with air. Twenty seconds after pressure was reduced to the initial level, the cat was switched over to breathing oxygen for the rest of the experiment.

In seven animals pulmonary pressure trauma was produced with air alone, which was breathed throughout the entire experiment. These experiments served as the controls.

Results

Table 1 shows the results of the first group of five experiments, where oxygen was breathed throughout.

TABLE 1

The effect of breathing oxygen on the resorption of gas emboli in blood vessels during pulmonary pressure trauma (intrapulmonary pressure was raised with oxygen)

Number of experiment	Quantity of gas in cannula trap with occurrence of pulmonary pressure trauma	Period of breathing oxygen	Quantity of gas in cannula trap at end of experiment	Characteristics of pathological picture found at autopsy
75	0.4—0.5 ml	32 min	0.4—0.5 ml	Gas bubbles in the medium-sized and small arteries, in the left atrium and ventricle, and coronary arteries
83	0.1 ml	60 min	6 gas bubbles	Several gas bubbles in the mesenteric arteries of the small intestines
80	1.2—1.4 ml	1 hr 36 min	2 gas bubbles	No gas in blood vessels or cardiac chambers
82	1.5—1.6 ml	2 hrs 25 min	20 gas bubbles	The same
85	1.5—1.6	2 hrs 45 min	21 gas bubbles	The same

Note. All the animals were in a satisfactory condition until the end of the experiment. Where the exact quantity of gas in the cannula trap could not be determined in ml, the number of gas bubbles found is given instead in the tables.

From Table 1 it is evident that with the occurrence of pulmonary pressure trauma 1 animal had about 40 gas bubbles (0.1 ml) in the cannula trap; 1 had about 0.5 ml of gas; and 3 had from 1.2 to 1.6 ml of gas. In one cat, which breathed oxygen for 32 min, no reduction in the quantity of gas was noted. Two cats breathed oxygen from 1 to 2 hrs; 2, from 2 to 3 hrs. In these 4 animals only several gas bubbles remained in the cannula trap at the end of the experiment. The animals were killed, and at autopsy the following was found: in 2 animals which had breathed oxygen for 32 and 60 min respectively, gas bubbles were found in the small and medium-sized arteries of the mesentery and small intestine, and in the coronary arteries; in the other 3, which had breathed oxygen for more than an hour, no gas was found in the blood vessels or in the cardiac chamber. No disturbance of respiration or circulation was found in any of the cats during the entire experiment.

In another group of experiments, five cats were switched over to breathing oxygen 20 sec after the occurrence of pulmonary pressure trauma (Table 2).

TABLE 2

The effect of breathing oxygen on the resorption of gas emboli in blood vessels in pulmonary pressure trauma (the intrapulmonary pressure was raised with air)

Number of experiment	Quantity of gas in cannula trap with occurrence of pulmonary pressure trauma (in ml)	Period of breathing oxygen	Quantity of gas in cannula at end of experiment	Condition of animal after completion of experiment	Characteristics of pathological pictures found at autopsy
99	0.1	1 hr 25 min	No gas	Satisfactory	In the blood vessels and in cardiac chambers gas was absent
103	0.1	1 hr 25 min	Same	Same	Same
96	0.1	2 hrs	"	"	"
89	0.6—0.7	2 hrs 55 min	"	"	"
98	0.6—0.7	2 hrs	1 bubble	Death	Several gas bubbles in the right atrium only

In Table 2 it is shown that in 3 out of 5 cats there were as many as 40—50 gas bubbles (0.1 ml) in the cannula traps; in 2 others, 0.6—0.7 ml. The first 3 cats breathed oxygen from 1 hr and 25 min to 2 hrs, and the gas bubbles of the cannula traps were completely resorbed. Two cats with a large quantity of gas in the cannula trap breathed oxygen for 2 hrs and 55 min. In one of them gas bubbles were resorbed; in the other, only 1 bubble remained, but the animal died, and the experiment was stopped. Four out of five cats remained in a satisfactory condition until the end of the experiment, and then were killed. At autopsy no gas was found in the blood vessels or cardiac chambers of these animals. In the cat which died several gas bubbles were found in the right atrium, but there was no gas in the arteries or veins of the body or internal organs.

In the third group of experiments 7 cats breathed air throughout the experiment (Table 3).

From Table 3 it is evident that in the third group of experiments pulmonary pressure trauma was accompanied by the entrance of no more than 40—50 gas bubbles (0.1 ml) into the cannula traps. Two out of seven animals were killed 55 min after increase in the intrapulmonary pressure. Until the end of the experiment the quantity of gas in the cannula trap remained practically unchanged. At autopsy gas bubles were found in the medium-sized and small arteries of the internal organs and body of the animal. There was no gas in the cardiac chamber. Two of the animals died after 1 hr and 11 min and 1 hr and 43 min. In the first the quantity of gas in the cannula trap remained as before; in the second, the gas was resorbed. At autopsy gas bubbles were found in both the mesenteric arteries of the small intestine. There was no gas in the other blood vessels and cardiac chambers. Three cats breathed air from 2 hrs 40 min

TABLE 3

The effect of breathing air on the resorption of gas emboli in the blood vessels in pulmonary pressure trauma (the intrapulmonary pressure was raised with air)

Number of experiment	Quantity of gas in cannula trap with occurrence of pulmonary pressure trauma (in ml)	Period of breathing oxygen	Quantity of gas in cannula trap at end of experiment (in cc)	Condition of the animal after completion of the experiment	Characteristics of the pathological pictures found at autopsy
52	0.1	48 min	0.1	Satisfactory	Gas bubbles in the medium-sized and small arteries. No gas in cardiac chambers.
59	0.1	55 min	0.1	Same	Same
107	0.1	1 hr 11 min	0.1	Death	Gas bubbles in the medium-sized and small arteries. Punctate hemorrhages under the epicardium along the course of the coronary blood vessels
115	0.1	1 hr 43 min	No gas	"	Several gas bubbles in the mesenteric arteries of the small intestine Punctate hemorrhages under the epicardium, along the course of the coronary vessels and mesenteric arteries of the small and large intestines
108	0.1	2 hrs 40 min	No gas	Satisfactory	Punctate hemorrhages confluent in places, forming hemorrhages the size of a kopeck coin, along the courses of the coronary vessels and mesenteric arteries of the small intestine
116	0.1	3 hrs	2 large bubbles and 10—15 very small ones	Same	Occasional gas bubbles in the small and large intestinal arteries. Punctate hemorrhages along the courses of the coronary vessels and mesenteric arteries of the small intestine
93	0.1	3 hrs 55 min	13 large bubbles and 10—15 very small ones	Death	Same

to 3 hrs and 55 min. In 1 the gas was completely resorbed toward the end of the experiment; in 2 others, the number of gas bubbles simply decreased. One of these 2 animals died; the other 2 were killed. In 1 out of 3 animals gas bubbles were found at autopsy in the mesenteric arteries of the large and small intestines. In the other 2 gas was absent from the blood vessels and cardiac chambers. Therefore, in only 2 out of 7 animals were the gas bubbles in the cannula trap resorbed as the experiment continued; in the other 5 the number of gas bubbles remained as before or decreased very slightly. In addition, on breathing air 3 out of 7 animals died.

At autopsy we found a characteristic feature; in all 5 cats which had breathed air for more than an hour, punctate hemorrhages the size of a pinhead were found under the epicardium, along the courses of the coronary vessels and in the vicinity of the mesenteric arteries of the small and large intestines. In some animals these hemorrhages became confluent, forming an area the size of a kopeck coin.

The mechanism of occurrence of these hemorrhages is unclear, but we believe they were formed at the place at which gas emboli were found, because none of the 10 animals breathing oxygen showed any hemorrhages. Probably, the very slow solubilization of gas bubbles during the breathing of air led to breaks in the blood vessels. As the result of this, at the sites of injury to the blood vessel wall blood extravasated into the surrounding tissues. The formation of a thrombus is difficult under such conditions, because the animals had first been given a large quantity of heparin.

Discussion of the Experimental Data

The results of our experiments showed that resorption of gas bubbles in the blood stream occurs more rapidly in animals breathing oxygen than in those breathing air. Usually 2—3 hrs of continuous breathing of oxygen was sufficient for the complete disappearance of gas bubbles from the cannula trap in the carotid artery and peripheral blood vessels. The change in the number of gas bubbles in the cannula trap corresponded essentially to the nature of changes in gas emboli in the animal's blood vessels. Resorption of gas bubbles occurs somewhat more slowly in the cannula trap than in blood vessels; at autopsy we frequently failed to find gas in the arteries, while gas bubbles were still being found in the cannula trap.

The experiments we performed with creation of pulmonary pressure trauma and arterial gas embolism permitted us to determine the effect of the nature of the gas mixture being breathed (oxygen and air) on the course of the disorder. Pulmonary pressure trauma and arterial gas embolism were observed in 30 [sic] animals.

Five out of 30 animals breathed oxygen during the experiment and remained in good condition (100%) until the end of the experiment.

In 8 [sic] animals pulmonary pressure trauma was produced by air pressure. Twenty seconds after the air pressure was reduced they were switched over to breathing oxygen. Four of them died (50%); the others remained in a satisfactory condition throughout the experiment.

During the entire experiments 17 [sic] animals breathed air. During the experiment 10 (58.8%) died; the rest were killed.

On the basis of the data presented it may be considered that the composition of the mixture being breathed exerts an influence not only on the resorption of gas bubbles in the blood stream but also on the subsequent course of pulmonary pressure trauma.

Conclusions

1. Pulmonary pressure trauma caused by an increase in oxygen pressure in the lungs with subsequent breathing of oxygen after reduction of pressure is distinguished by more favorable development than in the case of breathing air alone.

2. The breathing of oxygen for 2—4 hrs by animals with pulmonary pressure trauma and arterial gas embolism leads to complete absorption of gas emboli in the blood stream. In the case of breathing of air the solubilization of the gas bubbles occurs much more slowly, and at autopsy multiple hemorrhages are found in the animals along the courses of the coronary blood vessels, mesenteric arteries, of the small and large intestines, and those of other organs.

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Yu. M. Polumiskov

THE PROBLEM OF TREATMENT OF PULMONARY PRESSURE TRAUMA

(K voprosu o lechenii barotravmy legkikh)

The basic method for treating pulmonary pressure trauma is therapeutic recompression, as proposed by Polak and Adams (1932). However, in some cases this is impossible or too delayed. Therefore, great significance is ascribed to methods which can alleviate the patient's condition before recompression. We have been unable to find any experimental work along this line.

In performing experiments on the mechanism of occurrence of pulmonary pressure trauma we simultaneously studied the effect of active removal of excess gas (suction) from the intrapleural space into which the gas had entered through rupture of the lung tissue.

The experiments were performed on cats of both sexes. The method has been described in the article, "The Problem of the Mechanism of Occurrence of Pulmonary Pressure Trauma During the Breathing of Air and Oxygen", published in this collection. The gas was sucked out with a syringe through the side arm of a rubber tube connected into the system for recording the intrapleural pressure.

Results of the Experiments and Discussion

When pulmonary pressure trauma occurs in a cat the intrapleural pressure becomes positive, sometimes reaching 10—60 mm Hg. After reducing the intrapulmonary pressure which has caused the trauma, the intrapleural pressure decreases in 1—4 min, but almost always remains positive. As a rule, the animal develops dyspnea which is frequently accompanied by a fall in blood pressure and subsequent death.

For the purpose of improving the animal's condition and sometimes for reviving it we removed the excess gas by suction. The quantity of gas removed ranged from 20—2,000 ml in various experiments. The suction was stopped if the pressure in the suction system reached - 40—50 mm Hg. In Figure 1 a kymogram of experiment No. 92 dated 5 October 1960 is shown, which gives an idea of the changes occurring in pressure trauma of the lungs and of the effectiveness of using suction in this case.

As an illustration an abstract from the record is presented below.

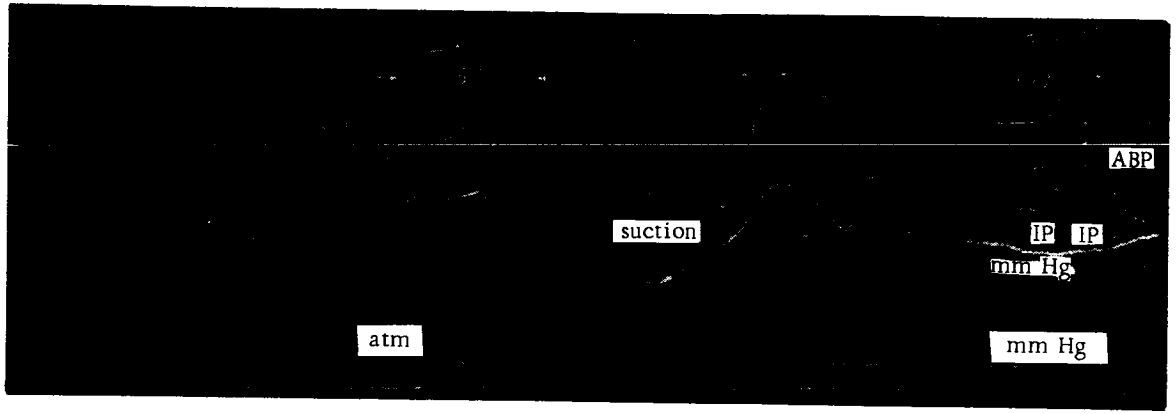


FIGURE 1. Explanation in the text
ABP — Arterial blood pressure; IP — intrapulmonary pressure

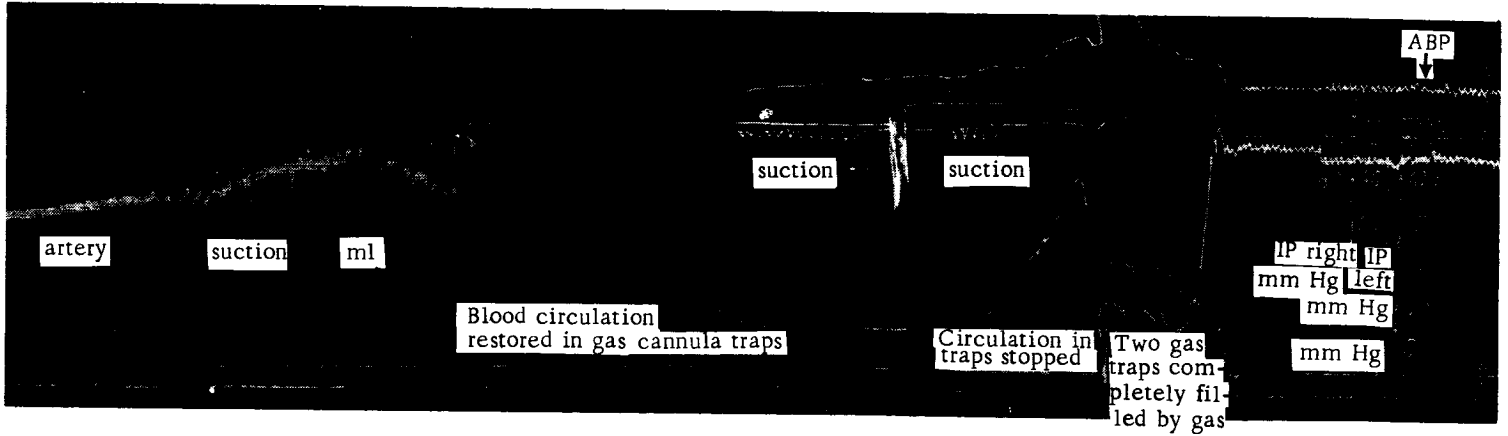


FIGURE 2. Explanation in the text

Record of Experiment No. 92 dated 5 October 1960

2.26 p.m. — blood pressure 115 mm; pulse, 156; respiration, 22, deep. The intrapleural pressure on right and left sides, 2 mm Hg.

2.27 p.m. — in 3 sec the intrapulmonary pressure rose to 120 mm, and was maintained at this level for 25 sec, after which it dropped in 1 sec to atmospheric pressure. When maximum intrapulmonary pressure was reached the blood pressure dropped to 40 mm; there was no pulse or respiration; the chest was expanded. The intrapleural pressure on the right pleural cavity was +96 mm; in the left, +100 mm. There was no gas in the cannula trap. The arterial blood was clear.

During the 60 sec following reduction of intrapulmonary pressure to atmospheric the blood pressure increased twice; apnea was noted, and the blood in the cannula traps was dark. At the same time, suction of gas from the right and left pleural cavities was begun with a syringe. Suction from the right cavity was stopped shortly afterwards because the pressure in the suction system fell to – 40 mm Hg.

Six minutes after the occurrence of pulmonary pressure trauma, when respiration and blood pressure became normal, suction was stopped. The blood pressure was 130 mm; the pulse, 132; respiration, 18 per min. Intrapleural pressure in the right pleural cavity was — 10 mm; in the left, — 4 mm. The animal was killed after 10 min.

At autopsy, pulmonary emphysema was found. The lungs were covered with a mass of punctate and focal hemorrhages. There were gas bubbles around the blood vessels of the lung roots. A considerable quantity of gas was present in the mediastinal tissue and tissue of the retroperitoneal space. There was no gas in the blood vessels or cardiac chambers.

Our experiments showed that suction of gas gives a definite positive effect in cases of severe pressure trauma of the lungs. When further suction proved impossible because of the marked reduction of intrapleural pressure, we used what we called "pumping" with this method, oscillations at a rate of 80—100 per min are made with the plunger of the syringe and pressure variations ranging from +30 to - 40 mm Hg are produced in the suction system.

By using "pumping" we attempted to renew the possibility of further suction. The mechanism of action of "pumping" is not yet entirely clear to us, but this measure, in a number of cases, made it possible to revive the animals.

In our experiments suction was used in animals with pulmonary pressure trauma after intrapulmonary pressure was increased from 60 to 200 mm Hg. The results obtained are shown in the table. In Figure 2 a kymogram is shown of experiment No. 82 of 9 August 1960.

From the kymogram it is evident that with increase of intrapulmonary pressure to 70—105 Hg both gas cannula traps were completely filled with gas. As a result of intrapulmonary pressure reduction a brief rise in the blood pressure was noted with a subsequent fall to 30 mm Hg. There was no pulse or respiration. The circulation in the traps stopped. The blood was dark. With the onset of the blood pressure drop, suction was begun from the left interpleural space; this was stopped shortly afterwards because of the marked reduction of pressure in the suction system. On the right side, suction was also impossible for this reason. Therefore, "pumping" was used on the right side, making possible renewed suction on the left side. Four minutes after suction slow circulation began in

the gas cannula trap. After 8 min suction was stopped. The blood pressure, pulse and respiration were completely restored.

TABLE

Results of using suction of gas from pleural cavities of an animal with pulmonary pressure trauma

Intrapulmonary pressure (in mm Hg)	Number of experiments	Results of use of suction in			
		pulmonary pressure trauma with arterial gas embolism		pulmonary pressure trauma without gas embolism	
		improvement of animal's condition	death	improvement of animal's condition	death
60—100	21	6	1	14	—
101—200	34	10	9	13	2
Total	55	16	10	27	2

As the table shows, suction was beneficial for 43 out of 55 animals (78.2%); the remaining 12 (21.8%) died. With pulmonary pressure trauma accompanied by arterial gas embolism, death was observed in 10 out of 26 animals (36.1%); without gas embolism, in 2 out of 29 (6.9%).

Therefore, the effectiveness of suction was considerably less in animals with pulmonary pressure trauma accompanied by gas embolism.

In experiments where intrapulmonary pressure was increased from 60—100 mm Hg the use of suction gave a positive result in 6 out of 7 animals (85.7%) with pulmonary pressure trauma and gas embolism in the blood vessels, and in all 14 with pulmonary pressure trauma without gas embolism. At the same time, the effect of [suction with a] pressure from 101—200 mm Hg provided an improvement in the conditions of 10 out of 19 animals (52.1%) with pulmonary pressure trauma and gas embolism, and in 13 out of 15 (86.6%) with pulmonary pressure trauma without gas embolism. Death occurred in 1 out of 21 animasl (4.8%) with increase in the intrapulmonary pressure from 60—100 mm Hg and in 11 out of 34 (32.4%) when the pressure created was from 101—200 mm Hg, i.e., the effectiveness of suction was reduced with increase in the intrapulmonary pressure.

To check the effectiveness of suction of gas from the pleural cavities in the more severe form of pulmonary pressure trauma, and to determine the role of arterial gas embolism in the results obtained, we used suction of gas in 50 experiments with repeated increases of intrapulmonary pressure without the occurrence of gas embolism. In these experiments the effect of gas emboli on the outcome of pulmonary pressure trauma was eliminated to a certain degree. Repeated increase in the intrapulmonary pressure was always accompanied by the additional entrance of gas into the pleural cavities, tissues of the mediastinum, neck, and retroperitoneal space, causing a deterioration of the course of pulmonary pressure trauma. In experiments with a repeated increase in the intrapulmonary pressure, suction failed to produce results in 2 out of 10 animals (20%) which had previously suffered from pulmonary pressure trauma with arterial gas embolism and in 7 out of 40 animals (17.5%) with pulmonary pressure trauma but without gas embolism.

On the basis of the data obtained we believe that the effectiveness of suction consists mainly of eliminating the effect of the associated pneumothorax on the course of pulmonary pressure trauma, and that it does not

eliminate the effect of arterial gas emboli on the animal organism.

Autopsy of the animals also showed that suction does not appreciably reduce the quantity of gas entering the interstitial spaces of the chest and abdominal organs when pressure trauma of the lungs occurs.

As a control, experiments without suction of gas were performed on 23 animals with pulmonary pressure trauma. In 7 of the 23 experiments the intrapulmonary pressure rose from 60 to 100 mm Hg; in 16, from 101—200 mm Hg. A comparison between the number of deaths which occurred in experiments using suction of gas and in control experiments shows the following: with increase in the pressure from 60 to 100 mm Hg 5 out of 54 animals died (9.2%) when suction was used, and 1 out of 7 (14.3%) died when it was not used; at pressures from 100—200 mm Hg 16 out of 51 animals (31.4%) died when suction was used, and 13 out of 16 (81.2%) died when it was not used. Thus, it is evident that suction of gas considerably reduces the number of deaths in animals in which the intrapulmonary pressure rose above 100 mm Hg.

"Pumping" was used in 15 experiments. In 6 animals it gave positive results; the other 9 died. We believe that marked variations in the intrapleural pressure in "pumping" produce an additional marked stimulation of receptors of the chest organs, contributing to recovery of the circulation and respiration.

In our opinion, the positive result attained from suction of the gas is explained by the fact that with the occurrence of pulmonary pressure trauma the gas enters the pleural cavities, mediastinal tissue, tissue of the retroperitoneal space and other organs. By suction the gas is readily removed from the interpleural spaces of both lungs, and probably a certain quantity of the gas is removed from the mediastinal tissue.

It may be supposed that suction creates a negative pressure in the interpleural cavity; the ruptured part of the lung is appressed against the parietal pleura and subsequently the lung can function under conditions which greatly correspond to those normally existing in the animal's body.

Removal of the excess gas not only eliminates the mechanical impediment to cardiovascular activity but also reduces the strength of stimulation of the receptors of the internal organs, which also has a positive effect. In some experiments, after a certain period of time, a positive intrapleural pressure recurred in the animals, accompanied by dyspnea. Repetition of suction in this case caused a rapid improvement in the animal's condition.

Conclusion

Active removal of the excess gas from the interpleural cavities of an animal with pulmonary pressure trauma assures an improvement in its condition without the use of therapeutic recompression.

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P. V. Oblapenko

THE ROLE OF PROPRIOCEPTIVE IMPULSES FROM THE CHEST AND ABDOMINAL MUSCLES IN THE REACTIONS OF THE BODY DURING RESPIRATION UNDER INCREASED INTRAPULMONARY PRESSURE

(Rol' impul'sov s proprioretseptorov grudnoi kletki i myshts zhivota v reaktsiyakh organizma pri dykhanii pod povyshennym davleniem v legkikh)

Through the studies of many authors (Coombs, Pike, 1922, 1930; W. Hess, 1931; Fleisch, 1930, 1931; Beccari, 1933; Sergievskii et al., 1950, 1958; and others) it was determined that reflexes from the proprioceptors of the muscles of the chest, diaphragm and rib joints participate in the regulation of respiration.

It was therefore natural to expect that in respiration under increased intrapulmonary pressure, the role of proprioceptive impulses in the reactions of the body increases.

The experiments of V. A. Vinokurov (1944, 1949) showed that after cutting the abdominal muscles in dogs under ordinary conditions of respiration the blood pressure drops 10—20 mm Hg, while cutting the abdominal muscles in vagotomized and desympathized animals leads to an even greater drop in blood pressure (by 30—50 mm Hg). During respiration under increased intrapulmonary air pressure of 200 mm H_2O, a preliminary section of the abdominal muscles led to slower stabilization of the blood pressure, and after additional vagotomy and desympathization no stabilization of the blood pressure occurred at all — on the contrary, it continued to drop progressively; the respiratory movements became slower, expiration lessened, and, finally, breathing stopped.

V. A. Vinokurov observed respiratory changes after increased air pressure in the lungs when the proprioceptive respiratory impulses had been partially excluded (only the abdominal muscles were cut). Therefore, it may be supposed that complete exclusion of the proprioceptive reflexogenic zones would lead to greater respiratory disorders, an assumption which is confirmed by data in the literature.

M. V. Sergievskii (1958), on the basis of clinical observations of B. Ya. Peskov, points out that with lesions of the cervical and thoracic portions of the spinal cord (in syringomyelia and syringobulbia), diaphragmatic respiration and asynchrony of synergistic respiratory muscles — external intercostal muscles and diaphragm — sometimes lessen markedly, even to the point of complete dissociation. Under experimental conditions a unilateral section of the posterior roots of the cervical and thoracic parts of the spinal cord of animals led to asynchrony of the respiratory movements of both sides of the chest.

Our observations of dogs with a low vagotomy showed that although the tone of their respiratory muscles decreased during breathing under increased intrapulmonary pressure (which was indicated by an increase in the size of the chest and abdomen), in the great majority of cases the strength of muscular contraction was sufficient for expiration.

This fact indicated that the reflexes which increase the tone of the respiratory muscles and lead to their contraction start not only from the pulmonary receptors (Popov, 1949; Kuznetsov, 1957; and others) but also from other interoceptive zones. Evidently, such reflex influences (trigger, tonicizing and corrective) also come from muscles and ligaments of the chest and abdomen. The experiments of V. A. Vinokurov and others have not provided a direct answer to this. Incidentally, V. A. Vinokurov, using section of the abdominal muscles, not only cut off the proprioceptive impulses but also injured the muscles themselves.

All the above data and our own observations indicated the need for a special investigation aimed at determining the role of increased proprioceptive impulses from the chest and abdominal muscles in the regulation of respiration and circulation with increased intrapulmonary pressure.

Method

The study consisted of short-term experiments on five dogs in which the flow of proprioceptive impulses to the central nervous system was first surgically cut off. The method of high section (at the level of the second cervical vertebra) of the posterior columns of the spinal cord (Goll and Burdach) was used; as is well known, these are the conductors of deep sensation (proprioceptive, vibrational and cutaneous two-dimensional). This method was used for studying the afferent systems in the laboratory of L. A. Orbeli as well as by L. S. Gambaryan (1953) for the study of conditioned reflexes from the propriocepter muscles and by V. P. Zagryadskii (1955) for determining the role of proprioceptive impulses in the course of hypoxemic convulsions.

The short-term experiments were performed on dogs 3—4 weeks (and in once case, a year) after such an operation.

The initial surgical preparation (to the time of cutting into the femoral vein for the injection of a hexenal solution) was carried out under brief superficial ether anesthesia. The entire subsequent preparation for the experiment and the experiment itself were conducted using hexenal anesthesia (calculating 40—60 mg/kg of body weight). During the experiment a record was made of thoracic and abdominal respiration, blood pressure in the femoral artery, pressure of the gas medium in the respiratory tract; in two experiments, blood pressure in the right ventricle was also determined.

Increase in intrapulmonary pressure was created by means of KPT or KP-24 oxygen apparatuses. The pressure amounted to 300—550 mm H_2O.

At the end of the experiments the spinal cords of the dogs operated on were checked anatomically and histologically.

Results of the Experiments

The results of the experiments performed on five dogs were unitypical. After increased intrapulmonary pressure in dogs with severed posterior columns of the spinal cord, all the basic changes in respiratory and circulatory functions characteristic of the initial period of respiration under increased intrapulmonary pressure were noted (apnea, and then slow respiration, marked decrease in the blood pressure, etc.). However, unique features were also noted.

As a result of the considerable loss of tone of the respiratory muscles of the chest and particularly of the abdomen at the time of increase of intrapulmonary pressure, a greater expansion of the chest and a marked enlargement of the abdomen occurred (Figure 1).

TABLE 1

Change in the respiratory rates of dogs with severed posterior columns of the spinal cord during respiration under increased intrapulmonary pressure

No. of experiment	Pressure (in mm H_2O)	Basic data	Respiratory rate (1 min)						Note
			after increase in pressure			after reduction of pressure			
			immediately	after 1 min	after 3 min	immediately	after 1 min	after 3 min	
1	550	8	apnea 14 sec	13	—	6	12	—	breathing air
2	550	8	apnea 25 sec	15	—	apnea 13 sec	14	11	same
3	400	12	4	6	6	8	13	12	breathing oxygen
4	300	10	apnea	apnea	apnea	8	10	10	same
5	300	11	apnea	"	"	10	12	12	"

The results of one of the experiments are shown on Figure 1. After prolonged respiratory arrest in inspiration following the increase in intrapulmonary pressure to 300 mm H_2O, expiration occurred only after 1.5 min; it was effected essentially by the chest muscles, whereas in normal animals the muscles of the abdominal press take a greater part in respiration. At the time of expiration a vigorous contraction of the chest muscles was observed; thereby the size of the chest decreased, and the volume of the abdomen increased. During inspiration, when the chest was expanded, the volume of the abdomen decreased markedly.

In the case of greater intrapulmonary pressures (Figure 2) asynchrony in the activity of the expiratory muscles of the chest and abdomen (and possibly also the diaphragm) was even more obvious. With a pressure equal to 550 mm H_2O the curves of movement of the chest and abdominal wall became mirror images of each other. It should be noted that in some experimental dogs, even during respiration under ordinary conditions, a

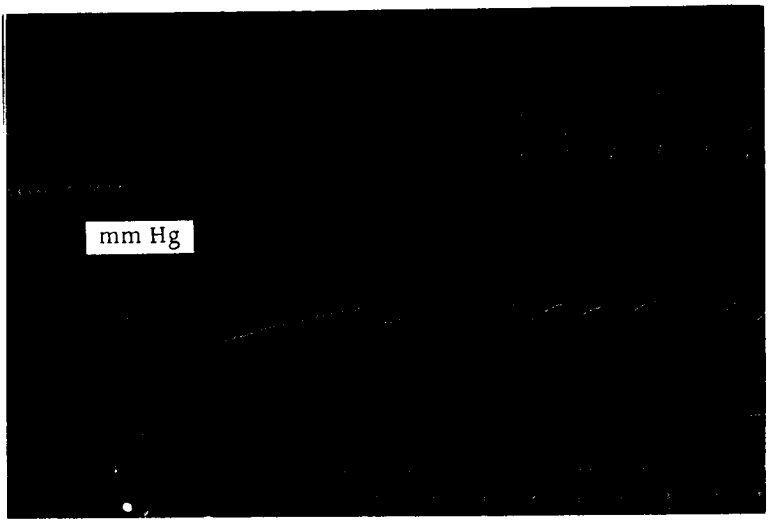


FIGURE 1. Characteristics of the change in respiratory movement of the chest and abdominal walls in a dog with severed posterior columns of the spinal cord during breathing under an excess pressure of 300 mm Hg. Experiment of 24 March 1958

From top down: thoracic respiration; abdominal respiration; blood pressure; base line of the blood pressure; time marking, two-second intervals; pressure in the respiratory tract (in mm H_2O); base line of the pressure in the respiratory tract (represented by the bottom margin of this figure).

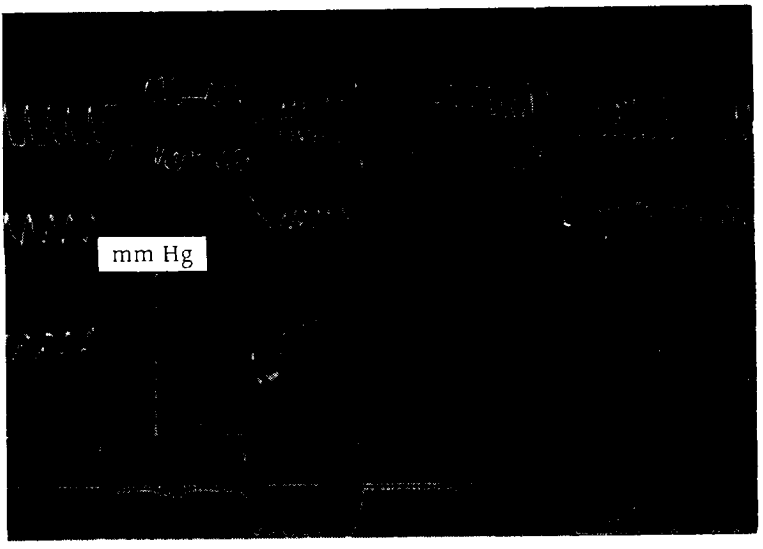


FIGURE 2. Characteristics of the change in respiratory movements of the chest and abdominal wall in a dog with severed posterior columns of the spinal cord during respiration under an excess pressure of 500—550 mm H_2O. Experiment of 13 March 1958

The keys for the curves are the same as for Figure 1.

disturbance of the synchronous activity of the external intercostal and abdominal muscles was observed. In dogs with intact proprioceptive conductors no such loss of coordination ever occurred in the activity of the chest and abdominal muscles.

Reduction of intrapulmonary pressure in animals with severed posterior columns of the spinal cord frequently caused a slowing of respiration or respiratory arrest, whereas in dogs with intact posterior columns of the spinal cord an appreciable increase in respiratory rate usually occurred (Table 1).

In dogs with severed columns of the spinal cord and with additional bilateral vagotomy an increase in the intrapulmonary pressure did not lead to apnea; conversely, their respiration became more frequent than in the initial state (Table 2). However, even after only 15—20 sec it not uncommonly began to slow up; the depth of the respiratory movements decreased and, finally, respiration apparently stopped with a weakening of expiration. After the fall of intrapulmonary pressure respiration was absent for a long time, and recovery of it began gradually, after about 30—50 sec (Figure 3).

TABLE 2

Change in the respiratory rates of dogs with severed posterior columns of the spinal cord and with bilateral vagotomy during respiration under increased intrapulmonary pressure

No. of experiment	Pressure (in mm H_2O)	Basic data	Respiratory rate (1 min)						Note
			after increase in pressure			after reduction of pressure			
			immediately	after 1 min	after 3 min	immediately	after 1 min	after 3 min	
1	550	8	16	2	—	apnea 30 sec	12	9	breathing air
2	550	8	12	1	—	apnea 25 sec	8	8	same
3	400	6	10	apnea	—	apnea	6	8	breathing oxygen
4	300	5	3	"	—	apnea 1 min 20 sec	2	4	same
5	300	4	3	"	—	apnea 45 sec	4	4	"

If apnea did not occur during the period of respiration under pressure, it occurred, of necessity, after the reduction of intrapulmonary pressure. As is well known from the papers of many authors, in the vagotomized dogs (with posterior columns of the spinal cord intact) intrapulmonary pressure reduction rarely causes apnea; usually, only a very slight retardation of respiration occurs.

Therefore, in our experiments asynchrony occurred in the activity of the respiratory muscles, similar to what is not uncommonly found in the

clinical picture of nervous diseases during syringomyelia and syringobulbia, and there was also a diminution of respiration (a factor first observed by V. A. Vinokurov (1944)).

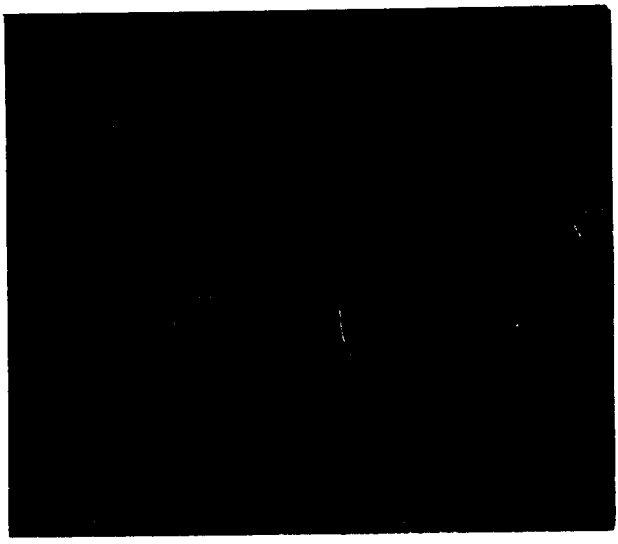


FIGURE 3. Change in the respiration and circulation in a dog with severed posterior columns of the spinal cord and with an additional vagotomy, during respiration under an excess pressure of 550 mm H_2O. Experiment of 13 March 1958

The key for the curves is the same as for Figure 1.

In dogs with severed proprioceptors a distinguishing feature of the circulatory changes during respiration under increased intrapulmonary pressure is the somewhat slower stabilization of the blood pressure. After additional vagotomy (both high and low) the circulatory changes were greater, and the blood pressure usually fell by 40—60 mm Hg. During the period of breathing under increased intrapulmonary pressure, stabilization of the initial hemodynamic changes occurred very slowly. After changing over to breathing under normal conditions the usual considerable blood pressure rise was not observed, and increase to the initial level occurred gradually.

This fact, as indicated above, was also noted by V. A. Vinokurov in vagotomized and desympathized dogs in which the abdominal muscle had been cut.

During the period of breathing under intrapulmonary pressure the blood pressure in the right ventricle increased less than in animals with intact posterior columns of the spinal cord.

Discussion of Results

The results of the investigation showed that in animals with severed proprioceptive tracts there was a marked reduction in the tone of the musculature of the abdominal wall and a coordination disorder in the activity of the external intercostal muscles and muscles of the abdominal press. These disorders are distinctly demonstrated under ordinary respiratory conditions and under increased intrapulmonary pressure, but they are particularly obvious after low and high vagotomy.

Our experiments show very clearly that during breathing under increased pressure reflex tension in respiratory muscles (particularly abdominal) is produced not only by interoceptive impulses coming from the lungs (Hess, 1931; Popov, 1949; Kuznetsov, 1957; and others) but also by proprioceptive impulses from the muscles and ligaments of the chest, abdomen and diaphragm. Thereby a very important role is played by tonic proprioceptive reflexes during respiration under increased intrapulmonary pressure.

The asynchrony of respiratory muscle activity observed can apparently be explained in the following way. At the end of inspiration the interoceptive impulses coming from distention of lung tissue cause a vigorous reflex contraction of the chest muscles for expiration. At the beginning of expiration the intrathoracic pressure rises; the diaphragm drops, displacing the abdominal organs downward. Because the tone of abdominal muscle is reduced they cannot prevent the ptosis of the diaphragm and abdominal organs, as a result of which the volume of the abdomen increases considerably.

With the beginning of inspiration the chest expands, and the intrathoracic pressure rapidly falls; the pressure in the abdominal cavity at this time evidently exceeds the intrathoracic pressure, the diaphragm is therefore displaced upward, and the size of the abdomen decreases. With the beginning of a new expiration this entire process is repeated in the same order.

In dogs which have also been vagotomized, exclusion of the interoceptive impulses naturally leads to an even greater hypotonia of the respiratory muscles and to a greater loss of coordination in their activity.

On the basis of the experiments presented it may be assumed that in animals in which the proprioceptive conductors have been cut, the activity of the respiratory muscles of the chest and abdominal press is effected essentially through reflexes from the pulmonary receptors. However, the activities of the various groups of respiratory muscles are not adequately coordinated with one another in the various phases of the respiratory cycle, particularly under increased intrapulmonary pressure. Tonic reflexes from the pulmonary interoceptors under these respiratory conditions do not assure the necessary muscle tone of the abdominal press and evidently are of less importance for these muscles than for those of the chest. The high degree of abdominal muscle tone required and fine coordination of their activity with that of the rest of the respiratory musculature may be assured by reflexes from both the interceptors of the lungs and proprioceptors of these muscles.

Of definite theoretical interest is why, in dogs with supplementary vagotomies, respiratory arrest occurs under increased intrapulmonary pressure, and also why apnea occurs after reduction of the pressure — a phenomenon very rarely encountered when vagus nerves are intact.

Using the data of V. A. Vinokurov and M. V. Sergievskii (1950) as a basis,

these facts may be explained in the following way. The proprioceptive impulses from the chest and abdominal muscles contribute to the formation of centrifugal impulses leading to a quickening and deepening of respiration in the respiratory center. In vagotomized animals with severed posterior columns of the spinal cord, it is essentially the proprioceptive and interoceptive impulses which are excluded; therefore, only some of the impulses from lungs continue to come to the central nervous system over the sensory fibers in the thoracic portion of the sympathetic nerves.

With increase in intrapulmonary pressure the greater flow of impulses passing over the afferent fibers of the thoracic sympathetic nerve from the pulmonary interoceptors to the respiratory center evidently causes an increase in the excitability threshold of the cells in the respiratory center connected with these fibers.

After reduction of the oxygen pressure the flow of impulses from the lungs decreases. The cells of the respiratory center during this period continue to function for a certain time at their previous reduced level of excitability. Therefore, ordinary impulses from the pulmonary mechanoceptors are inadequate for restoring the respiratory center to an active state, as the result of which apnea continues. Respiration does not recur until excitability of the cells in the respiratory center is raised to the level at which impulses of ordinary strength can bring them to an active state.

As for blood pressure changes, they are essentially induced by reduction of abdominal muscle tone, which leads to a deterioration of the conditions necessary for the inflow of venous blood into the right heart. However, in animals in which only the posterior columns of the spinal cord have been cut, just as in animals which have been vagotomized only, the circulatory disorders are not demonstrable to such a degree as in animals in which both operations have been performed. In the latter, with the marked reduction in abdominal muscle tone, the intraabdominal pressure is evidently reduced to such a degree when it does not assure adequate return of the venous blood to the heart even under normal respiratory conditions; thereby the blood pressure decreases markedly (by 40–60 mm Hg).

With respiration under increased intrapulmonary pressure, when increased tonic contraction of the abdominal muscle is required for overcoming the intrathoracic pressure obstructing the blood movement from the inferior vena cava to the right heart, the marked reduction of abdominal muscle tone does not entirely assure the indicated function. In this connection, the blood pressure in the right ventricle increases less than in animals which have only been vagotomized or in which the posterior columns of the spinal cord have been cut. However, arterial pressure, as a rule, is not compensatory and remains very low or even continues to decrease. Also of great significance is the absence of the sucking action of the thorax during inspiration.

Changes in blood circulation are approximately the same. In dogs with severed posterior columns of the spinal cord and high vagotomy (when the normal cardiac innervation is impaired), and with low vagotomy (when the cardiac innervation is not impaired), the changes in the blood circulation are approximately the same. This indicates that such pronounced circulatory disturbances under these conditions result basically from the marked decrease of blood inflow to the heart due to the sharp reduction of the abdominal muscle tone.

Conclusions

1. During respiration under increased intrapulmonary pressure the exclusion of the proprioceptive impulses by the complete severing of the posterior columns of the spinal cord of dogs causes reduction of tone and contraction of respiratory muscles, and leads to loss of coordination of the thoracic and abdominal muscles. The reduced tone of respiratory muscles and their asynchronous activity after supplementary vagotomy is markedly expressed.

2. The sharp reduction of abdominal muscle tone observed in animals after the posterior columns of the spinal cord have been cut and supplementary vagotomy performed causes, even under normal conditions, a considerable decrease in the blood pressure level (by 40—60 mm Hg). During respiration under increased intrapulmonary pressure recovery from the initial hemodynamic disorders is very slow or does not occur and the pressure in the right ventricle increases significantly.

3. In dogs in which the proprioceptive impulses have been cut, during respiration under increased intrapulmonary pressure, a supplementary high or low vagotomy causes approximately the same circulatory disorders. This indicates that the basic factor leading to serious circulatory disorders under these conditions is the significant decrease of blood flow to the right heart due to the sharp reduction of abdominal muscle tone, and the exclusion of the sucking effect of the thorax during inspiration.

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P. V. Oblapenko

THE CONDITION OF VASCULAR REFLEXES IN DOGS DURING RESPIRATION UNDER INCREASED INTRAPULMONARY PRESSURE

(Sostoyanie sosudistykh refleksov u sobak pri dykhanii pod povyshennym davleniem v legkikh)

In studies by P. M. Gramenitskii and co-authors, V.P.Popov, A.G.Subbota and others, it has been shown that breathing under increased intrapulmonary pressure is accompanied by considerable hemodynamic disorders, as the result of which the blood pressure falls in some parts of the blood stream and rises in others. It is perfectly obvious that in the reactions directed at maintaining the blood pressure at a constant level, reflexes from the various vascular receptor areas, chiefly the carotid and aortic areas, play a relatively unimportant part.

The determination of the condition of the vasomotor reflexes and their part in the reactions during respiration under increased pressure is of definite theoretical and practical significance for a more correct evaluation of the body functions under these conditions. Nevertheless, there are only occasional papers in the literature which give data on the condition of the vascular reflexes and the significance of the vascular reflexogenic areas in the recovery of the impaired circulatory functions during respiration under increased pressure.

V. I. Popov (1949) in experiments on two rabbits, and A. G. Subbota (1956) in experiments on cats, determined that cutting the nerves of the carotid sinus and aortic reflexogenic areas, particularly after additional bilateral vagotomy, has a negative effect on the restoration of the blood pressure level. However, the authors did not study the condition of the vascular reflexes themselves.

Only Kim Don Sok (1958) in experiments on cats determined the fact that the pressor reflexes (reflexes to compression of carotid arteries, painful and ammoniacal stimulation of the trigeminal nerve) are altered during increased intrapulmonary pressure; usually they disappear and are even inverted. The endocrine glands exert an effect on the nature of change in these reflexes. On the basis of these investigations the author concluded that during respiration under increased intrapulmonary pressure the pressor component of vascular reflexes does not occur in the compensatory reactions of the body directed at stabilization of the blood pressure.

Thus, in the literature there is controversial data on the participation of the vascular pressor reflexes in the body's compensatory reactions during respiration under increased intrapulmonary pressure, and there is absolutely no data on the condition of the depressor reflexes.

The aim of our investigation was to study the nature of the changes in the carotid sinus pressor and depressor reflexes, and to clarify their significance in the body's adaptive reactions under these respiratory conditions.

Method

The study was made in short-term experiments on dogs under superficial hexenal anesthesia (25—40 mg/kg body weight for the entire experiment). Through a mask or tracheotomy cannula the animals breathed under increased pressures of oxygen (or air) which was created by means of oxygen apparatuses (KP-24 and KP-T); the pressure in the respiratory tract did not exceed 400 mm H_2O. The condition of the vascular reflexes was judged by the pressor and depressor effects after compression of both carotid arteries, as well as after stimulation of the sinus nerve with an induced current. The distance between the primary and secondary windings of the induction coil in various experiments ranged from 12 to 25 cm; in each individual experiment the distance between the windings was constant.

The vascular reflexes in dogs were studied each time before the beginning of respiration under increased intrapulmonary pressure, and then in the intervals between the first and second, second and third, and third and fifth minutes after increasing the pressure and in changing over to normal pressure conditions. If respiration under intrapulmonary pressure lasted over 5 min the reflexes were investigated in the 7th and 10th minutes.

Results of the Experiments and Discussion

The results of the experiments are shown in Tables 1 and 2.

As is evident from Table 1, in the initial state after compression of both carotid arteries, the blood pressure in all experiments increased appreciably (by an average of 50 mm Hg with individual variations in the pressor reaction from 18 to 90 mm Hg).

During respiration under increased pressure the pressor effect after compression of the arteries decreased appreciably and was directly related to the blood pressure level at the time of the investigation: the higher the blood pressure level the more pronounced the pressor reaction (Figures 1 and 2).

In view of the fact that the lowest blood pressure level was observed in the first minute after increasing the intrapulmonary pressure, it is obvious that the pressor reaction at this time was minimal. Eventually, with increase in the blood pressure, there was an increase in the pressor reaction.

Thus, for example, in experiments Nos. 3a and 5, compression of the carotid arteries in the 2nd minute of breathing under pressure caused a rise in the blood pressure—in experiment 3a, by 22 mm Hg; in experiment 5, by 6 mm Hg. In the 4th minute of compression, when the blood pressure level rose, the pressor effect also increased in experiment 3a, from

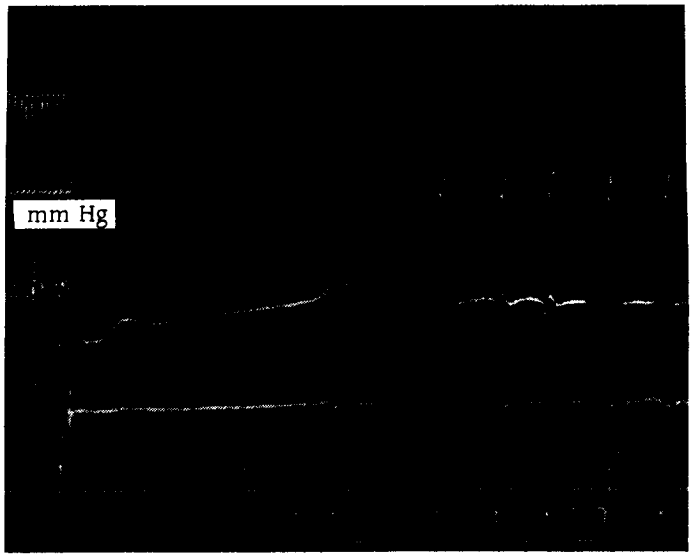


FIGURE 1. Condition of the pressor carotid reflex in a dog with high blood pressure level during respiration of oxygen under increased intrapulmonary pressure. Experiment of 22 February 1958.

From top down: thoracic respiration; abdominal respiration; blood pressure; blood pressure in the right ventricle; base line of the blood pressure and time marking of compression of carotid arteries; base line of blood pressure in right ventricle, time marking—two-second intervals; pressure in the respiratory tract (in mm H_2O); base line of the pressure in the respiratory tract.

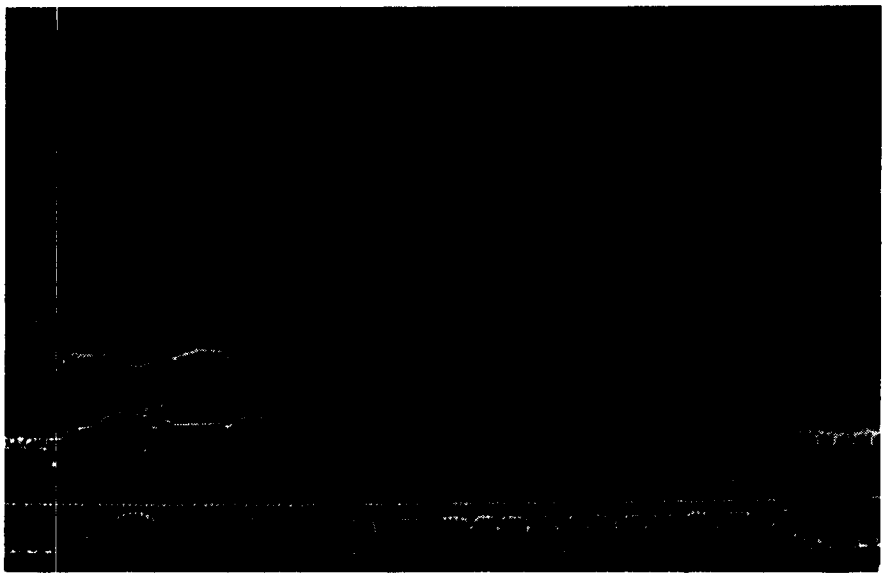


FIGURE 2. Condition of the pressor carotid reflex in a dog with a low blood pressure level during respiration of air under increased intrapulmonary pressure. Experiment of 20 February 1958

The key is the same as for Figure 1.

TABLE 1

Measurements of blood pressure and heart rate in dogs after compression of the carotid arteries during respiration under increased intrapulmonary pressure

No. of experiment	Intrapulmonary pressure (in mm H_2O)	Indices of physiological functions	Control data		During respiration under increased pressure				After reduction of intrapulmonary pressure			
					after 1—2 min		after 3—5 min		after 1 min		after 3 min	
			basic data	during compression of carotid artery	basic data	during compression of carotid artery	basic data	during compression of carotid artery	basic data	during compression of carotid artery	basic data	during compression of carotid artery
1	300	Blood pressure (in mm Hg)	132	162	108	122	—	—	150	200	—	—
		Number of heart beats per min	140	168	196	208	—	—	120	136	—	—
2	250	Blood pressure (in mm Hg)	150	212	100	130	—	—	—	—	—	—
		Number of heart beats per min	120	136	148	200	—	—	—	—	—	—
2a	400	Blood pressure (in mm Hg)	146	202	70	80	—	—	—	—	—	—
		Number of heart beats per min	124	142	188	188	—	—	—	—	—	—
3	350	Blood pressure (in mm Hg)	136	186	120	152	120	150	—	—	—	—
		Number of heart beats per min	128	160	168	184	160	184	—	—	—	—
3a		Blood pressure (in mm Hg)	136	196	58	80	140	170	130	180	—	—
		Number of heart beats per min	140	156	128	134	128	152	126	144	—	—
4	400	Blood pressure (in mm Hg)	140	170	50	50	—	—	140	172	—	—
		Number of heart beats per min	108	120	208	208	—	—	160	176	—	—
5	300	Blood pressure (in mm Hg)	140	158	72	78	136	150	—	—	136	152
		Number of heart beats per min	80	88	136	144	120	128	—	—	104	112
6	300	Blood pressure (in mm Hg)	88	106	60	66	82	90	88	118	90	120
		Number of heart beats per min	160	168	168	176	168	184	192	192	176	184
6a	400	Blood pressure (in mm Hg)	90	106	60	66	88	96	106	134	106	134
		Number of heart beats per min	160	168	208	216	108	108	184	200	168	184

22 to 30 mm Hg; in experiment 5, from 6 to 13 mm Hg. In experiment No. 3, in which the blood pressure level in the 2nd and 4th minutes remained the same (120 mm Hg) the pressor reaction was also the same (30 mm Hg).

The rise in blood pressure after compression of the carotid arteries in the 2nd minute amounted, on the average for all experiments to 16 mm Hg (as against 50 mm in the initial state); in the 4th minute, the pressor reaction increased to 24 mm. After switching over to normal atmospheric pressure the pressor reaction increased and reached the initial figures.

As is well known, the rise in blood pressure after compression of the carotid arteries is accomplished by two reflex reactions — vasoconstriction and increase in the heart rate. In the initial condition, as follows from Table 1, the heart rate after compression of the carotid arteries increased by 8—32 beats (by 18, on the average). Therefore, participation of the cardiac component in the pressor reaction under normal respiratory conditions was perfectly obvious.

After switching over to increased pressure, compression of the carotid arteries was not always associated with an increase in cardiac activity. This was the case in those experiments where the heart rate at the time of compression was very rapid — about 200 per min (experiments Nos. 2a, 4, 6, and 6a). The pressor reaction was brought about essentially only through vasoconstriction, and was less in its magnitude than in cases where an increase in cardiac activity was observed in addition to vasoconstriction. For example, in experiment No. 4 compression of the carotid arteries did not lead to an increased blood pressure, and in experiments Nos. 2a, 6, and 6a the pressor reaction was very slight (6—10 mm). The results of our experiments (reduction and even disappearance of the pressor reaction) agree considerably with the data of Kim Don Sok, although we did not observe the inversion of carotid sinus reflexes which occurred in his experiments. Despite the similarity of the facts obtained, however, we do not agree with Kim Don Sok's conclusion that during respiration under increased intrapulmonary pressure there is no pressor component in the compensatory reaction of blood pressure stabilization. As our experiments show, the pressor reaction of the blood vessels does occur whenever there is reduced blood pressure. However, the pressor effect is less pronounced than under ordinary conditions, which is evidently connected with a reduction in the blood volume in the arterial system of the greater circulation.

During breathing under increased pressure the depressor reaction changed to a greater degree than the pressor reaction.

After releasing the pressure from the carotid arteries in the initial condition the blood pressure usually fell quickly, and after several seconds returned to the initial level or even dropped somewhat below it (Figure 1). With breathing under pressure the depressor reaction was observed only where the blood pressure level had been comparatively high before investigation of the reflex; at a low blood pressure, as indicated above, the pressor reaction was slight, and the depressor reaction was entirely absent.

To ensure more reliable conclusions about the condition of the depressor reflex reaction, the sinus nerve was stimulated with an induced current. The results of these experiments are shown in Table 2.

As follows from Table 2, the degree of the depressor reaction depends, first of all, on the initial blood pressure level, and secondly, on the degree

TABLE 2

Changes in blood pressure and heart rate in dogs after stimulation of the sinus nerve with an induced current during respiration under increased intrapulmonary pressure

No. of experiment	Intrapulmonary pressure (in mm H_2O)	Indices of physiological function	Control data		During respiration under increased pressure				After reduction of intrapulmonary pressure			
					after 1-2 min		after 3-5 min		after 1 min		after 3 min	
			basic data	on stimulation of the sinus nerve	basic data	on stimulation of the sinus nerve	basic data	on stimulation of the sinus nerve	basic data	on stimulation of the sinus nerve	basic data	on stimulation of the sinus nerve
1	300	Blood pressure (in mm Hg)	120	60	70	60	94	68	102	78	102	88
		Number of heart beats per min	138	114	138	126	138	138	108	126	150	150
1a	300	Blood pressure (in mm Hg)	130	94	—	—	50	40	78	54	—	—
		Number of heart beats per min	210	210	—	—	210	210	210	210	—	—
2	400	Blood pressure (in mm Hg)	136	80	42	40	76	68	—	—	—	—
		Number of heart beats per min	112	96	184	184	162	162	—	—	—	—
3	300	Blood pressure (in mm Hg)	140	110	—	—	140	88	—	—	132	82
		Number of heat beats per min	96	80	—	—	112	80	—	—	104	80
4	400	Blood pressure (in mm Hg)	120	48	114	70	106	80	136	130	—	—
		Number of heart beats per min	112	80	160	146	152	152	100	100	—	—
4a	400	Blood pressure (in mm Hg)	112	50	106	92	122	119	130	86	124	66
		Number of heart beats per min	112	88	184	176	160	120	104	72	112	80
4b	400	Blood pressure (in mm Hg)	110	76	102	88	—	—	116	118	—	—
		Number of heart beats per min	176	168	192	192	—	—	168	168	—	—

Note. Results of experiments 1a and 4b -- after atropinization.

of slowing of cardiac activity with stimulation of the sinus nerve. The lower the blood pressure at the time of the investigation and the less the participation of the cardiac component in it, the less pronounced the depressor reaction. In a number of experiments a pressor rather than a depressor reaction was observed during stimulation of the sinus nerve at the time of maximum blood pressure reduction.

In other experiments, at the beginning of the nerve stimulation the blood pressure rose, and only near the end or after cessation of stimulation did it begin to decrease. In these cases retardation of cardiac activity did not occur or was very slight.

It is characteristic that after atropinization of animals as well as after vagotomy the depressor effect also fell off sharply, and in some experiments it was entirely absent or was distorted (Table 2, experiments Nos. 1a, and 4b).

The same changes in the carotid sinus pressor and depressor reflexes in rabbits were observed by V. L. Gubar' (1952) after polarization (with a cathode) of the medulla with direct current. Artificial increase in the tone of the vasoconstrictor center changed its reflex activity. According to the data of this author, compression of the carotid arteries and stimulation of the aortic nerve under these conditions had little effect on the blood pressure level. Increase in the excitability of the vasoconstrictor center with an electric current interfered with the development of a reflex increase or decrease in the blood pressure level.

We are inclined to explain these characteristics in the change in pressor and depressor carotid sinus reflexes during breathing under increased pressure by the fact that the vasoconstrictor center at a low blood pressure level is evidently in a state of persistent excitation, that is, in a state of a dominant focus (Magnitskii, 1952). It is entirely possible that a certain degree of anemization of the brain contributes to this standing excitation of the center, as indicated by the experiments of P. P. Goncharov and I. R. Petrov. In 1934 they, and the co-workers of I. R. Petrov (Antipenko, 1950; Kudritskaya, 1952; Zor'kin, 1955; and others) proved that in anemization of the brain, shock and blood loss where reduction of blood was observed, first the depressor and then the pressor reflexes disappeared. The authors explain these changes in the vascular and cardiac reflexes by a change in the interrelationship of excitatory and inhibitory processes in the corresponding brain centers. The initial loss and inversion of the depressor carotid sinus reflex with the pressor reflex intact was considered by I. R. Petrov an adaptive reaction. It is possible that during respiration under increased pressure the omission of the depressor reflex and even an inversion of it is also an adaptive reaction of the body.

The question of the interrelationship of vasomotor and respiratory centers during respiration under increased intrapulmonary pressure is of great theoretical interest.

As was pointed out in our article (Oblapenko, 1964), the respiratory center is in an inhibited state immediately after the increase in intrapulmonary pressure and not uncommonly for some time thereafter (for several minutes). The vasomotor center is in a state of excitation from the first moment, when there is a sharp drop in the blood pressure in the aorta. It is possible that immediately after the increase in intrapulmonary pressure a brief irradiation of inhibition occurs from the respiratory to the vasomotor center; however, the latter evidently eliminates this effect comparatively quickly. This is confirmed by the following observations.

In some experiments the initial, comparatively sharp rise in blood pressure led to the occurrence of inspiration and restoration of respiration after apnea. In cases of prolonged apnea compression of both carotid arteries along with blood pressure rise not uncommonly led to a renewal of respiration (Figure 1). Stimulation of the sinus nerve, conversely, caused respiratory arrest.

Therefore, whereas the normal interrelationship between the vasomotor center and the respiratory center is usually characterized by the predominance of the latter's effects, the reverse situation is encountered during breathing under increased intrapulmonary pressure, i.e., the vasomotor center has the greater effect on the respiratory center.

Conclusions

1. During breathing under increased intrapulmonary pressure the carotid sinus pressor and depressor reflexes in dogs decrease. The depressor reflex is more variable.
2. The degree to which the magnitudes of these reflexes are reduced depends on the blood pressure level in the greater circulation, which is essentially determined by the tone of the vasoconstrictor center.
3. With a very low blood pressure, as well as after atropinization of animals or vagotomy, the pressor carotid sinus reflex is minimal, and the depressor effect may disappear completely or even be distorted.
4. During the period of considerable reduction of blood pressure in the greater circulation there is irradiation of excitation from the vasomotor to the respiratory center, which at this time is in an inhibited state. This contributes to a more rapid recovery of respiration in the initial period after increase of intrapulmonary pressure.

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P. V. Oblapenko

THE ROLE OF THE VAGUS NERVES IN THE BODY REACTIONS DURING BREATHING UNDER INCREASED INTRAPULMONARY PRESSURE

(O roli bluzhdayushchikh nervov v reaktsiyakh organizma pri dykhanii pod povyshennym davleniem v legkikh)

Presently, oxygen apparatuses constitute one of the means of providing oxygen to flight crews under increased intrapulmonary pressure due to break in the airtight ceiling of the airplane cabin during stratosphere flights.

Although apparatuses supplying oxygen to the respiratory system under increased pressure began to be used in aviation practice only in the 1940's, the study of the effect on the body of increased intrapulmonary air pressure was begun long ago. The Valsalva test with increase in intrathoracic pressure, used in clinical medicine to determine the functional condition of the cardiovascular system, was well known even in the mid- 18th century. Experimental studies aimed at determining the effect on the body of breathing air under increased pressure and the mechanisms of respiratory and circulatory changes observed during this process were begun at the start of the 1860's (Einbrodt, 1861). A particularly large number of papers were written on this subject after the method of breathing oxygen under increased intrapulmonary pressure had been used in 1943 for improving the body's oxygen supply at altitudes above 12,000 m (Cagge, Allen, et al., 1945; Barach et al., 1946, 1947; Popov, 1949; Ivanov and Novak, 1949; Kuznetsov et al., 1952, 1957; Vakar, 1953; Botvinnikov, Gramenitskii, et al., 1955; Subbota, 1956; Grandpierre, et al., 1957; Jacquemin et al., 1958; Kim Don Sok, 1958; and others).

Despite the large number of studies made on the effect on the body of increased oxygen (or air) pressure in the lungs, the matter of mechanisms of change in respiratory and circulatory functions remains unclear and the data on some problems is even controversial. Thus, for example, there is no agreement in the literature as to the role of the vagus nerves during respiration under these conditions.

The majority of authors believe that the vagus nerves participate in adaptive reactions and increase the body's resistance to this factor (Botvinnikov, Gramenitskii, et al., 1955; Subbota, 1956; and others). Conversely, others point out that the elimination by vagotomy of reflex influences through the vagus nerves contributes to an improvement in the condition of the body (Popov, Kuznetsov, Gorev, and Cherkasskii, 1955; Kondratovich, 1956; and others).

In the present work, a more detailed study was made of the role of of the vagus nerves in the circulatory and respiratory reactions during

increased intrapulmonary pressure, using instruments which supply oxygen or air to the lungs.

Method

For the purpose of solving the problems posed we used low vagotomy — below the point at which centrifugal cardiac nerves branch off, together with high section of the vagus nerves in the neck of dogs. This method was necessary because of the fact that high vagotomy previously used by many authors not only interrupted the flow of afferent impulses from the lungs and abdominal organs to the central nervous system but at the same time interfered with the normal innervation of the heart, since the latter was deprived of parasympathetic influences. This fact has been overlooked by many authors.

The experimental study was carried out in short-term experiments on 20 dogs 3—5 years of age. Thirty to forty minutes before the experiment was begun the animals were given a subcutaneous injection of a 2% morphine hydrochloride solution in a dose of 1.0—1.5 ml/10 kg body weight. The femoral vein was dissected out under brief ether stupefaction, and then an intravenous injection of 2% hexenal solution was given. During the experiment, which lasted 1.5—2 hrs, an average of 1.5—2.5 ml of hexenal solution/kg body weight was given.

In preparing the animals for the experiment, the femoral artery, vagus nerves from the lower margin of the larynx to the point at which the cardiac branches branch off, and the right jugular vein were dissected out.

To prevent coagulation of the blood in the cannulas, heparin was given intravenously in a dose of 0.2—0.25 ml/10 kg body weight. A glass tube, which was connected through a rubber tube with a Ludwig mercurial manometer, was introduced into the right ventricle of the heart through the jugular vein. The entire preparation for the experiment took 40—60 min.

In the initial state and during the course of the experiment a record was made of the blood pressure in the femoral artery and in the right ventricle, thoracic and abdominal respiration, and the air or oxygen pressure in the respiratory tract. Increased air or oxygen pressures in the respiratory system was created by means of KP-24 and KP-T oxygen apparatuses. The dogs either breathed through a tracheotomy cannula or through a mask with a compensating outlet valve specially prepared for them.

The oxygen apparatus for breathing under increased pressure was used in one or two sessions, from 3—10 min in all variants of the experiments; in various experiments breathing under pressure was continued without interruption for as long as 30 min. The pressure in the respiratory system was 200—250 and 300—400 mm H_2O.

Results of the Experiments

In dogs with intact vagus nerves the following reactions occurred immediately after increase in the air or oxygen pressure in the lungs (Figure 1): respiratory slowing or arrest lasting from a few score seconds to several minutes; expansion of the chest and abdomen; fall of the blood

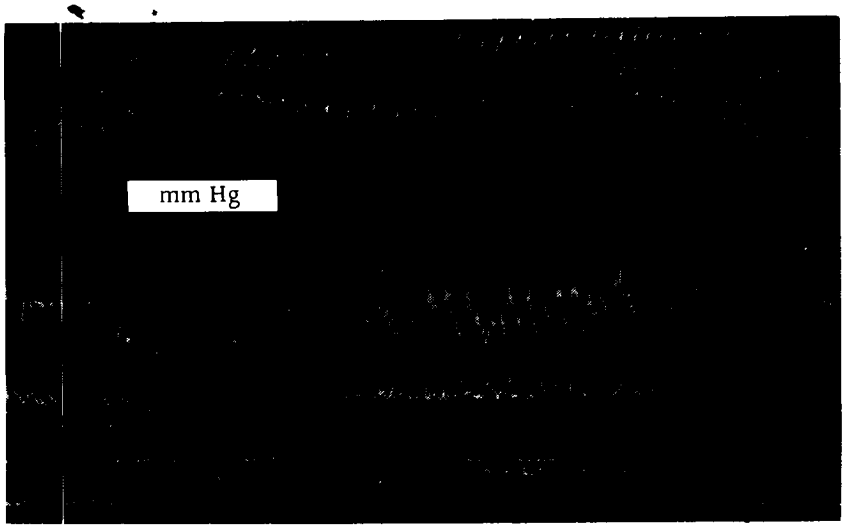


FIGURE 1. Respiratory and circulatory changes in a dog before vagotomy during the breathing of air under an intrapulmonary pressure of 400 mm H_2O. Experiment of 17 January 1958

From top down: thoracic respiration; abdominal respiration; blood pressure in the femoral artery; blood pressure in the right ventricle; base line of the blood pressure; time marking—two-second intervals; air pressure of the respiratory tract; base line of pressure in respiratory tract. Arrows from left to right, beginning and end of increase of intrapulmonary pressure.

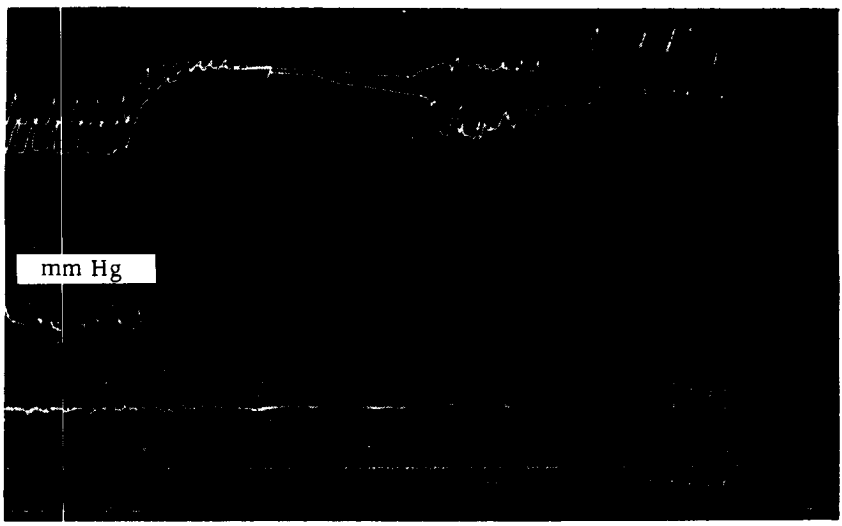


FIGURE 2. Respiratory and circulatory changes in a dog after high vagotomy during the breathing of air with an intrapulmonary pressure of 400 mm H_2O. Same experiment.

From top down: thoracic respiration; abdominal respiration; blood pressure in the femoral artery; base line of the blood pressure; blood pressure in the right ventricle; base line of the pressure in the right ventricle; time marking; air pressure in the respiratory tract; base line of the pressure in the respiratory tract.

pressure in the greater circulation; increase of the blood pressure in the right ventricle; and slowing or (less often) a slight increase in the heart rate.

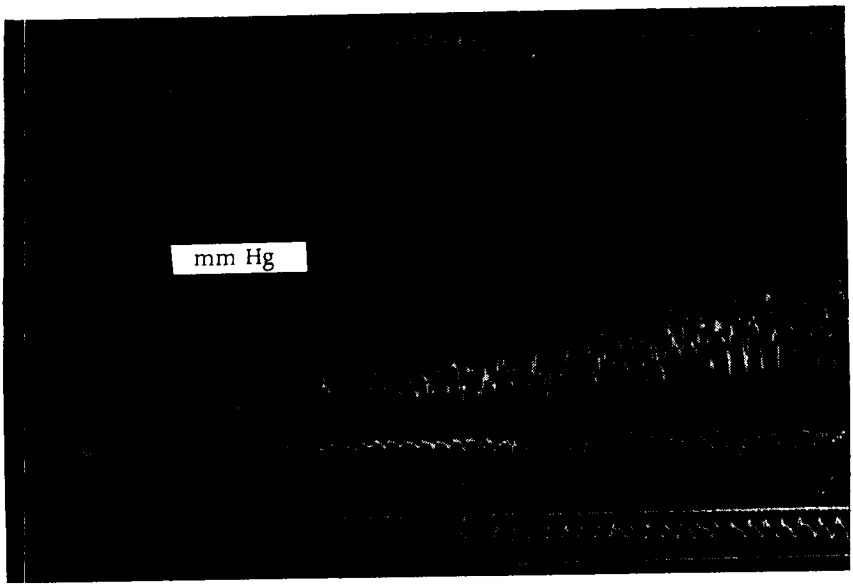


FIGURE 3. Respiratory and circulatory changes in a dog after low vagotomy during the breathing of air with intrapulmonary pressure of 400 mm H_2O. Same experiment.

The key for the curves is the same as for Figure 1.

Subsequently, in most experiments the rate and depth of respiration were gradually restored to normal, although respiration was usually slower than in the initial condition and was not always rhythmical; the blood pressure leveled off; the pulse increased in frequency; the blood pressure in the right ventricle continued to be elevated.

After switching over to normal breathing conditions there was a reduction in the volume of the chest and abdomen, and normalization of the rate and depth of respiration occurred; the blood pressure was initially markedly increased, and then it approached the initial level in an undulating manner; the pulse slowed considerably at first but returned to the initial rate comparatively quickly; the pressure in the right ventricle fell immediately but shortly afterwards, as the result of an increase in the amplitude and strength of its contractions, the systolic pressure increased. Recovery of the respiratory and circulatory functions occurred, as a rule, within 3—5 min.

Regardless of whether oxygen or air was used for breathing under pressure, no differences in principle in the circulatory or respiratory reactions were observed.

With increase in intrapulmonary pressure, dogs subjected to high vagotomy showed a greater expansion of the abdomen than before vagotomy; respiration did not slow up but, conversely, increased slightly in rate;

in most cases the blood pressure dropped somewhat more slowly but it leveled off slowly also, and with high intrapulmonary pressures not uncommonly no elevation of the blood pressure was observed at all (Figure 2). Increase in the pressure in the right ventricle and change in the heart rate were less than before vagotomy.

In dogs with low vagotomy, even before the increase in intrapulmonary pressure, not uncommonly a change in the heart rate in the direction of both increase and decrease was observed. The circulatory changes showed certain characteristic features. Only in 30% of the cases did the pulse rate remain unchanged after low vagotomy. The blood pressure remained at almost the same level as before vagotomy; only at times were slight changes observed in it, brought about, evidently, by changes in the heart rate. Increase in the intrapulmonary pressure leads to essentially the same respiratory changes as in cases with high vagotomy.

As is evident from Figure 3, when the breathing apparatus was used under increased pressure in dogs with a low vagotomy the blood pressure at first dropped quickly also; it leveled off more slowly than before vagotomy but more rapidly than after high vagotomy. A change in the heart rate and pulse pressure occurred after a certain delay. At first, the pulse slowed up a little or remained unchanged, but after some seconds (10—20) it increased in rate. The amplitude of the pulse waves at first also decreased appreciably and was lowest at the time the blood pressure reached the lowest level. Almost simultaneously with the rise in blood pressure and increase in pulse rate, the pulse waves gradually enlarged. At this time we also noted an increase in tension of the abdominal muscles, which, however, was less pronounced than before vagotomy. The pulse rate reached its maximum 1—2 min after increase in intrapulmonary pressure, but was usually less than in experiments with high vagotomy. After this the amplitude of the pulse waves continued to increase or remained unchanged, and the pulse began to slow up, as was also the case before vagotomy. The blood pressure continued to increase or remained at the previous level. The pressure in the right ventricle in a number of experiments increased to a lesser degree than before vagotomy.

After reduction of intrapulmonary pressure to normal the general picture of recovery of circulatory functions was approximately the same as it had been before vagotomy.

For the purpose of interrupting the parasympathetic fibers of the vagus nerves without impairing the integrity of the afferent tracts, we performed four experiments with atropinization of the animals, which were given an intravenous injection of 2 ml of 0.1% atropine solution. These experiments showed that after increase in the intrapulmonary pressure, tachycardia was more pronounced than in dogs with high vagotomy, reaching 200 or more beats per minute. The blood pressure did not always come up to the level which had been observed in the dogs before atropinization. Only at low pressure levels was there no difference.

Discussion of Results

Increased pressure in the respiratory system, like other unusual factors, causes, on the one hand, changes in the body indicating a functional disorder

and on the other, adaptive, protective reactions directed at placing the organism in equilibrium with the new conditions.

Although it is very difficult to make a detailed analysis of the mechanisms of these complicated reactions, one fact is beyond doubt: in many of these reactions the vagus nerves played a very great part. Thus, for example, respiratory slowing or arrest, constantly observed in short-term experiments on animals in the initial period of respiration under increased intrapulmonary pressure, is explained by all authors studying this problem by the inhibitory effect of afferent impulses passing over the vagus nerves to the respiratory center.

The brief bradycardia, which contributes to a more marked drop in blood pressure, may be explained as a reflex inhibition of cardiac activity from the pulmonary receptors through the afferent and efferent fibers of the vagus nerves. Evidently, a second reflex acting along the same line is that from the pulmonary arteries described by Schwiegk (1935) and V. V. Parin (1941). V. V. Parin believes that blood pressure reduction in the arteries of the greater circulation when there is increased pressure in the pulmonary arteries is a function of two components: 1) a cardiac component — slowing of the rate, and 2) a vascular component — dilatation of the arteries of the greater circulation. Vagus nerve fibers also represent an afferent component of this reflex.

In our experiments, animals with a high vagotomy showed no such slowing of the heart rate immediately after increase in intrapulmonary pressure. At the same time, in many experiments after low vagotomy the slow heart rate remained. In the latter case, despite the exclusion of the pulmonary receptor area, afferent impulses from the pericardium and great vessels (over the depressor nerve) continued to go to the central nervous system over the vagus nerves; this afferentation was entirely sufficient to inhibit cardiac activity.

In the case of breathing under increased pressure no greater than 400—500 mm H_2O, the comparatively brief period of respiratory and circulatory disorders is usually followed by a period of their recovery. Constant stimulation of the vagus nerves by increased impulses from the chest and abdominal organs interferes, as a rule, with the complete recovery of respiratory rate. Low and high vagotomy eliminate the inhibitory effect on the respiratory center but not in all cases. Slowing of respiration, which was sometimes observed in our experiments even after vagotomy, indicates the existence of other afferent pathways from thoracic organs. They may be sensory fibers in the thoracic portion of the sympathetic nerve or in the posterior roots of the spinal cord (Vinokurov, 1944).

In our experiments the blood pressure was restored most rapidly and completely in dogs with intact vagus nerves. The main reflex mechanisms contributing to stabilization of the blood pressure and increase in the heart rate were reflexes from the carotid sinuses and aortic area. V. I. Popov and A. G. Subbota have proved the importance of these reflexes for the stabilization of blood pressure during breathing under increased intrapulmonary pressure.

A greater increase in the heart rate was observed in experiments with lower intrapulmonary pressures (up to 250—300 mm H_2O), and in some experiments tachycardia developed immediately after the increase in intrapulmonary pressure without preliminary bradycardia. Undoubtedly,

a definite part in the increase in heart rate was played by the reflex from the ostia of the venae cavae because of the increase of the blood pressure in them (Pavlov, 1874; Bainbridge, 1915), and by the reflex connected with inflation of the lungs (Saalfeld, 1932). That both these reflexes have vagus fibers as the afferent component is confirmed by the fact that after high vagotomy of dogs, we did not observe any great acceleration of the heart rate. This has also been noted by all authors who have studied this problem.

In the case of breathing under increased pressure after low vagotomy the increase in heart rate also occurred as a rule, although in a number of cases it was less pronounced than before the procedure. Our explanation for this is that after low vagotomy reflexes from the lung tissue and blood vessels accelerating the heart rate were interrupted, and only reflexes from the ostia of the venae cavae, aorta and carotid sinuses continued to function.

Evidently, in the case of breathing under increased intrapulmonary pressure the significance of the vagus nerves as regulators of the diastolic period of the heart increases considerably. It is perfectly clear that with the increased load on the right ventricle created by elevated intrapulmonary pressure cardiac fatigue should be greater. Hence, it is natural that in almost all nonvagotomized dogs and in those with low vagotomy, tachycardia was replaced several minutes after the pressure increase by an appreciable slowing of the heart rate without any reduction in blood pressure. This reaction should be regarded as adaptive, directed at maintaining cardiac efficiency under these conditions.

From this viewpoint another phenomenon becomes easily explainable. In dogs with a high vagotomy or after atropinization, particularly in experiments with high values of intrapulmonary pressure, blood pressure stabilization was not always observed. Despite the fast heart rate, which came to 200—240 beats per min, the blood pressure remained very low or even continued to drop, threatening the animal's life. In these cases a switch had to be made to normal pressure; nevertheless, in various experiments the animals died several minutes after the intrapulmonary pressure drop (Figure 2).

Therefore, during breathing under increased intrapulmonary pressure after high vagotomy, the heart, deprived of parasympathetic inhibition of its rate, quickly became extremely fatigued. For a long time the right ventricle was incapable of overcoming the resistance to the blood flow in the pulmonary capillaries and of driving the blood into the left heart; the blood pressure therefore failed to increase or even dropped to zero, while there was an increase in venous stasis. In such cases, the replacement of tachycardia by bradycardia toward the end of the experiments indicated a marked reduction of the functional capacity of the heart due to fatigue, and was not an adaptive reaction.

Our experiments with atropinization also prove the favorable nature of parasympathetic effects on cardiac activity in breathing under increased pressure.

Therefore, the experiments showed that the poorer tolerance of animals with a high vagotomy to breathing air or oxygen under intrapulmonary pressure as high as 400 mm H_2O is caused by the less perfect reflex regulation of cardiac activity. Cutting the vagus nerves in the neck leads

to interruption of the reflex which slows cardiac activity and makes myocardial rest more difficult. There are also indications that the vagus nerves, aside from their retarding effect on the heart, also mediate trophic influences which increase ventricular contractions (Smirnov, 1952).

During breathing under increased pressure the tone of the abdominal musculature acquires exceptional importance. By means of this reflex, which is also increased with the participation of afferent fibers of the vagus nerves (Vinokurov, Popov, Kuznetsov, and others), not only is expiration carried out, but the inflow of blood into the right heart is also improved (Vinokurov, 1944; Subbota, 1956).

It is perfectly obvious that the cardiovascular reactions alone, which contribute to a more rapid passage of blood from the right heart into the left, are inadequate when there is considerable resistance in the blood vessels of the lesser circulation. It is essential in addition, to provide the proper inflow of venous blood into the right atrium. Without this, increased work of the right ventricle will be wasted, without realizing its proper effect. Reflex tension of abdominal muscles during expiration, which is rhythmically replaced by relaxation during inspiration, contributes to the more rapid passage of blood through the abdominal portion of the inferior vena cava (in animals, the posterior vena cava) toward the right heart.

Our experiments with low vagotomy, where venous return to the right heart is made more difficult, showed that despite the comparatively perfect reflex regulation of cardiac activity the blood pressure leveled off more slowly. Evidently, in these cases there was an interruption of the physiological mechanism of reflex increase in the tone of the abdominal muscles. After high vagotomy, resulting in both deterioration of conditions for the inflow of blood into the right atrium and impairment of regulation of cardiac activity (the parasympathetic influences were interrupted), there was no recovery of the deranged circulatory functions in a number of cases.

Conclusions

1. With a change to breathing under increased intrapulmonary pressure, dogs show respiratory inhibition and reduction of the heart rate, contributing to a fall in the blood pressure in the greater circulation, brought about by afferent impulses coming from the mechanoreceptors of the lungs and other thoracic organs over the vagus nerves.
2. The stabilization of blood pressure which occurs subsequently is effected by a number of reflexes; the vagus nerves constitute the afferent component of the reflex arc of this process.
3. The parasympathetic fibers coming to the heart through the vagus nerves inhibit the rate of cardiac contractions, increase the duration of diastole, and, thereby, reduce cardiac fatigue during breathing under increased pressure.
4. Low vagotomy results in a reduction of abdominal muscle tone, a deterioration of venous inflow into the right heart, and a slower compensation for the hemodynamic changes caused by increased intrapulmonary pressure, by comparison with nonvagotomized animals.

5. High vagotomy, which causes, in addition, a disruption of the reflex regulation of cardiac activity, produces a considerable impoverishment of the animal's tolerance to breathing under increased pressure.

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RESPIRATORY AND CARDIOVASCULAR REFLEXES FROM GASTROINTESTINAL MECHANORECEPTORS IN BAROMETRIC PRESSURE CHANGES

(Refleksy s mekhanoretseptorov zheludochno- kishechnogo trakta na dykhanie i serdechno- sosudistuyu sistemu pri perepadakh barometricheskogo davleniya)

It is well known that a considerable drop in barometric pressure (as in decompression of airplane cabins and emergence from deep water) sometimes results in abdominal pain with labored respiration, cardiac disorders, and even loss of consciousness, due to expansion of the gas and increase of pressure in the stomach and intestines (Brestkin, 1944; Pivovarov and Komendantov, 1946; Skrypin, 1948; and others). Development of protective measures against these disorders has been impeded by the insufficient data concerning their physiological mechanisms. Only occasional papers (Ivanov, 1944; Chirkin, 1955, 1958) offer facts suggesting a reflex origin of the reactions to local dilatation of the stomach and intestines investigated by these authors during barometric pressure changes.

Therefore, the aim of our investigation was a study of the physiological mechanisms of the effect of dilatation of the gas in the entire gastrointestinal tract during barometric pressure changes.

Method

The study was made on dogs in two series of long- term and short- term experiments: 1) experiments in which air was introduced into the gastrointestinal tracts in the animals; 2) experiments with barometric pressure changes.

Three fistulas — of the stomach, small and large intestines — were placed on each dog before the long- term experiments and during the short- term experiments. A study was made of changes of respiration, blood pressure, and pulse rate, and the gas pressure in the stomach and intestines was recorded (separately in each section in some experiments; in the others the same pressure was maintained in all parts of the gastrointestinal tract). In the first series of experiments respiration was recorded from the animal's chest ("thoracic" respiration) and from the anterior abdominal wall ("abdominal" respiration); in the last series, from the trachea through a tracheotomy cannula. In the long- term experiments a record was also made of the volume of pulmonary ventilation. In all short- term

experiments and in a number of long-term experiments the blood pressure was recorded from the femoral artery and its branches by means of a mercurial manometer. The experiments were conducted in a pressure chamber at both normal and reduced barometric pressure. In all, 67 experiments were performed on 43 dogs.

Experimental Data

The effect of introducing air into the gastrointestinal tract. The aim of this series of long- term and short- term experiments was to study the characteristics of simultaneous mechanical stimulation of all parts of the gastrointestinal tract, similar to that which occurs during barometric pressure changes. Before administration of air the basic data was recorded for 2 min, and then the volume of air recorded by the experimental conditions (from 1.5 to 10 l under a pressure of 10—20 mm Hg) was introduced for a period of 2 min into the gastrointestinal tract through the fistulas from a tank through a reducer and a gas meter. After this, the fistulas were closed for 2 min, and the gas remained in the gastrointestinal tract. The gas was released through the fistulas for 2 min also. In this series 28 experiments were performed on four dogs.

Data of long- term experiments. In most cases air administration did not cause any apparent reaction of the animals adapted to the experimental conditions, and only in some cases, with a gas pressure higher than 20 mm Hg, did they show behavior changes, ranging from a mild motor reaction and whining to vigorous movement.

In 32 cases out of 45, respiration increased in frequency (by 10—55%) at the beginning of air administration (Table 1); when the gas pressure in the stomach and intestines increased to 15—20 mm Hg it became slower, irregular, and uneven, with a drawn- out stepwise expiration. Sometimes even respiratory arrest was observed for 8—10 sec. With the entrance of gas into the gastrointestinal tract the chest expanded somewhat, and its respiratory movements became more superficial. The amplitude of the respiratory movements of the abdominal wall increased sharply at first and then, when the pressure was highest in the gastrointestinal tract (15—20 mm Hg), particularly in the stomach, this increase was replaced by a marked decrease. As soon as some of the air went from the stomach into the duodenum, which could be judged by the corresponding change in gas pressure in each of these sections, abdominal respiration again increased considerably. After introduction of air, in most cases the volume of pulmonary ventilation increased simultaneously in all parts of the gastrointestinal tract, chiefly because of increased respiratory rate. When the gas was released from the gastrointestinal tract the chest assumed its usual size; the abdominal wall was retracted; abdominal respiration decreased markedly, and the depth of thoracic respiratory movements increased. The respiratory rhythm became regular. Respiration gradually returned to its initial form (Figure 1). However, cases were noted (7 out of 45) where air administration was accompanied by reduction in the frequency and increase in the amplitude of thoracic respiration, as well as reduction in the amplitude of abdominal respiration. In 6 cases the respiration did not change.

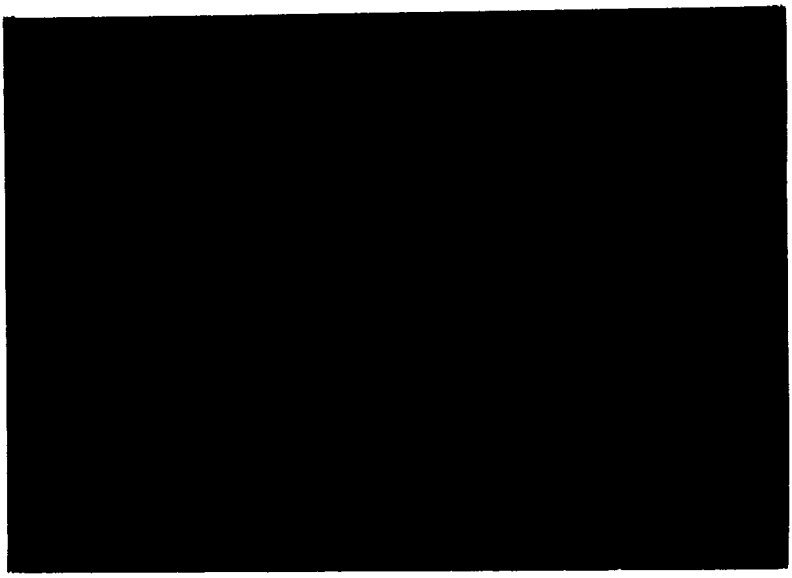


FIGURE 1. Changes in thoracic and abdominal respiration after introduction of air into the gastrointestinal tract in a long-term experiment of 7 April 1949

Tracing components (from top down): thoracic respiration; abdominal respiration; gas pressure in the gastrointestinal tract; marking of the volume of pulmonary ventilation; marking of stimulation (1st—beginning of air administration; 2nd —cessation of air administration; 3rd—beginning of its release); time marking, five-second intervals.

In 28 out of 34 cases the pulse rate increased (by 5—30%) after the introduction of air into the gastrointestinal tract; in 5, it slowed, and in one case remained unchanged (Table 2). After gas administration was stopped the pulse slowed up somewhat. Its slowing continued even after the release of the gas from the gastrointestinal tract. Only later did the pulse gradually return to its initial level.

After introduction of air into the gastrointestinal tract the blood pressure in all 6 experiments rose (by 8, 16, 18, 36, 48, and 66 mm Hg), and the pulse and respiratory waves became smaller. Pressure changes in the gastrointestinal tract were always accompanied by parallel variations in respiration, pulse rate and blood pressure level. With release of the gas the blood pressure returned to the initial level.

It is characteristic that the perfectly distinct changes in respiration, pulse rate and blood pressure were observed equally often in cases of pronounced motor reactions and of absence of movements. Therefore, they cannot be explained by the movements of the experimental animals.

Data of short-term experiments. The aim of performing short-term experiments in this series was to determine the nature of blood pressure changes under gas pressures of 30 and 40 mm Hg, which could not be done in long-term experiments because of the marked motor reactions of the dogs, and to determine the role of the "mechanical" (elevation of the diaphragm, shift of the cardiac axis, compression of the great vessels of

TABLE 1

Respiratory rate in dogs with introduction of air into the gastrointestinal tract

Date of experiment	Name of dog	Respiratory rate per min					
		Control before air administration	by minutes after air administration				
			1st	2nd	3rd	4th	5th
20 XII 1948	Al'fa	16	20	21	26	23	—
24 XII	Bobik	15	16	18	15	—	—
8 III 1949	"	15	15	15	—	—	—
10 III	"	14	18	17	17	17	12
		12	18	17	17	14	—
		10	12	—	12	12	12
12 III	"	12	15	16	11	12	12
		12	16	20	15	12	12
		13	15	13	14	13	14
		13	15	15	14	15	14
15 III	"	15	16	16	15	14	13
		14	15	14	14	14	14
17 III	"	13	14	13	13	13	12
		12	17	17	16	17	15
		13	19	25	18	16	14
19 III	"	13	17	16	15	13	13
		13	18	14	17	15	13
22 III	"	13	14	13	14	13	11
24 III	"	12	14	16	16	15	12
25 III	Barynya	13	13	18	11	12	14
		13	18	10	9	10	12
29 III	Bobik	12	16	17	14	16	13
31 III	Barynya	14	19	15	15	16	14
1 IV	Bobik	13	22	23	19	20	19
4 IV	Barynya	17	19	17	17	18	14
8 IV	"	17	18	16	21	16	19
9 IV	"	14	15	16	16	13	10
12 IV	"	19	21	27	27	27	24
15 IV	"	19	19	23	22	21	23
19 IV	"	18	22	23	23	21	28
		25	27	29	30	33	28
		24	27	24	27	28	28
21 IV	"	22	24	22	21	25	23
		16	17	17	15	18	18
		20	21	25	26	31	30
26 IV	"	35	37	41	41	47	32
30 IV	"	19	23	20	19	20	21
5 V	Al'fa	62	67	72	78	78	50
		37	57	69	67	—	29
6 V	Chernysh	14	14	13	10	13	14
		12	15	13	12	14	12
7 V	Al'fa	31	41	34	18	28	15
		23	38	46	40	53	13
		23	44	47	48	53	32
		31	39	86	82	22	15

TABLE 2

Pulse rate in dogs after introduction of air into the gastrointestinal tract

Date of experiment	Name of dog	Respiratory rate per min					
		Control before air administration	by minutes after air administration				
			1st	2nd	3rd	4th	5th
19 III 1949	Bobik	70	85	80	90	—	—
		120	160	110	—	—	—
		120	140	110	120	—	—
24 III	"	83	80	108	100	120	88
25 III	Barynya	96	120	120	106	106	96
		90	120	126	126	108	108
		90	90	78	90	90	108
29 III	Bobik	100	120	126	132	150	120
		120	138	126	132	150	136
		105	144	144	126	120	120
		108	126	120	138	135	105
31 III	Barynya	90	120	120	96	84	96
1 IV	Bobik	90	126	120	120	108	102
		90	126	—	120	120	114
		96	68	67	64	64	90
		102	108	110	120	120	102
4 IV	Barynya	96	120	120	96	96	108
		90	132	132	120	108	120
		102	130	126	120	126	108
		102	84	96	108	120	108
8 IV	"	102	96	108	102	90	120
		90	102	84	108	102	108
9 IV	"	108	132	126	108	96	105
		109	120	123	120	126	115
12 IV	"	84	96	96	80	84	96
		96	108	120	138	108	108
15 IV	"	96	116	118	110	116	120
21 IV	"	96	108	108	108	102	90
		84	64	68	72	78	88
		111	150	147	114	132	120
26 IV	"	90	102	114	90	96	80
		102	114	120	108	114	114
30 IV	"	100	120	104	104	108	120
		120	112	136	160	146	128

the abdominal cavity) and reflex components. In short-term experiments air was administered 74 times in 16 dogs. The experiments were performed under intravenous urethane anesthesia (0.8—1.0 g of a 20% urethane solution per kg body weight).

The introduction of air into the gastrointestinal tract under these conditions caused in the majority of cases distinct respiratory and blood pressure changes which were essentially similar to those in long-term experiments. However, the latent period of the reaction was somewhat longer (as long as 15—20 sec). In addition, it developed that air administration under great pressure (30—40 mm Hg) does not cause an initial increase in the respiratory rate, as we observed under a pressure equal to 10—20 mm Hg, but usually slows it immediately. The increase in frequency sometimes occurred later. As in the long-term experiments, increased blood pressure was a characteristic reaction (15 out of 22 cases). In 3 cases it did not change; in 4, it decreased. Cases of blood pressure reduction coincide with a considerable reduction in respiratory rate and with apnea, and evidently depend on them. The blood pressure changes usually began somewhat later than the respiratory changes, but both always followed all gas pressure variations in the gastrointestinal tract (Figure 2).

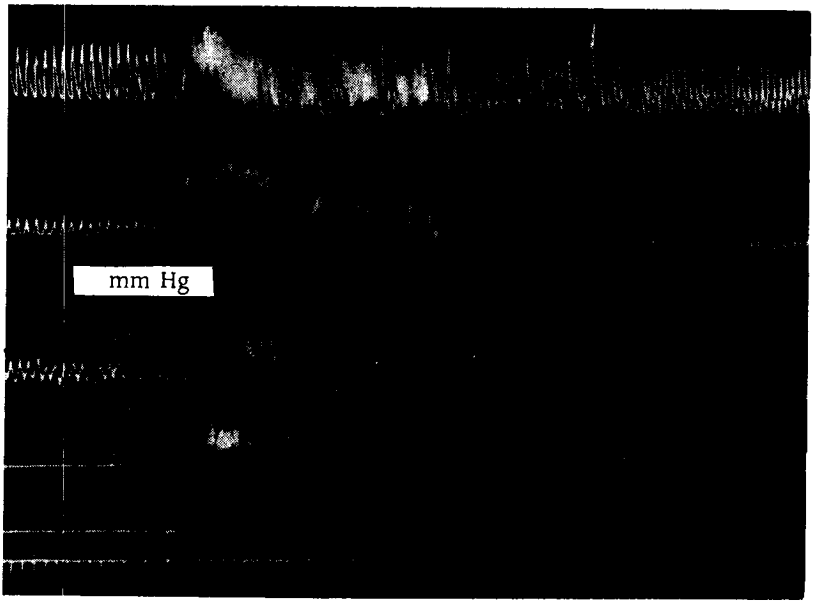


FIGURE 2. Changes in respiration and blood pressure after introduction of air into the gastrointestinal tract in a short-term experiment of 17 May 1949. The order of the tracings is the same as in Figure 1 but without recording of the volume of pulmonary ventilation.

Introducing the gas separately through the gastric or one of the intestinal fistulas showed that the greatest changes in respiration and blood pressure are produced by dilatation of the stomach. This reaction was almost exactly the same as the response to simultaneous introduction of air into all 3 fistulas in this experiment.

In subsequent experiments a reaction to the introduction of air under a pressure of 10 mm Hg with increased or reduced tone of the gastrointestinal tract was demonstrated. Increase in tone was produced by the administration of small doses of acetylcholine or physostigmine intravenously; decrease, by the local action of adrenalin or atropine. The respiratory and blood pressure reactions were of the same type and equal in degree both after the increase and decrease in tone, and corresponded to the results of a control administration of air if the gas pressure remained the same. Hence, the reaction to the air administration depends essentially on the pressure created rather than on the initial level of gas to intestinal tone.

The next problem was to determine the significance of the "mechanical" and reflex components in the origin of the reaction being described.

For the purpose of determining the role of the "mechanical" component the air was introduced with the abdominal cavity widely open and with the small intestine exteriorized and placed in a bath containing physiological saline solution. The experiments showed that the reaction to air administration, at leased under the degrees of pressure we created (as high as 10 mm Hg), remained just as distinct as in the controls, i.e., it cannot be completely determined by mechanical effects on the diaphragm, heart or great vessels, although a shift of the cardiac axis and an elevation of the cupola of the diaphragm sometimes occur, as our separate experiments with fluoroscopy of the animals showed.

To determine the role of the reflex component of the reaction, air was administered 35 times after cutting the vagus and splanchnic nerves and after novocain block of the abdominal nerve plexuses.

Cutting the vagus nerves under the diaphragm led to lesser changes in respiration and blood pressure from introduction of air into the gastrointestinal tract, particularly into the stomach: the first period of slowing of respiratory depression and fall in blood pressure was eliminated, the latent period of the respiratory reaction was markedly prolonged, and the motor reaction of the gastrointestinal tract was less pronounced. It appears, therefore, that the initial period of respiratory depression and reduction of blood pressure in the case of introduction of the air is brought about by the vagus nerves, essentially through the afferent impulses from the gastric receptors. The second phase of the reaction — increase of respiratory rate and elevation of blood pressure — are produced only partly by the action of the vagus nerves; after vagotomy the reaction decreased but never disappeared.

Cutting of the splanchnic nerves altered less than vagotomy the nature of the respiratory and blood pressure reactions to introduction of air into the gastrointestinal tract, only slightly lessening it and sometimes distorting the nature of the changes in blood pressure.

Even simultaneous section of the vagus and splanchnic nerves did not completely prevent changes in respiration and blood pressure from the introduction of air into the gastrointestinal tract, though it did produce a marked lessening of the reaction.

Therefore, the splanchnic nerves and vagus nerves were subsequently cut with simultaneous infiltration of the abdominal nerve plexuses with a novocain solution. Introduction of air after this caused absolutely no change in the blood pressure, and a barely noticeable respiratory reaction, which

could have depended on the preservation of the phrenic nerves and perhaps part of the posterior root innervation. This showed definitely that the reflex mechanism is basic not only in the case of local mechanical stimulation of the gastrointestinal tract, which has been shown in a number of physiological investigations (Goncharov, 1945; Kurtsin, 1952; and others) but also after a general mechanical stimulation of the tract. The reaction begins not only from the mucosal receptors but from the mechanical receptors of all layers of the stomach and intestines, as is evidenced by the fact that novocain anesthesia failed to prevent the changes described.

The effect of gas expansion in the gastrointestinal tract during barometric pressure changes. In all, 170 ascents were carried out in a pressure chamber in short-term experiments on 23 dogs. During the ascent in the chamber barometric pressure was reduced to 354—267 mm Hg, which corresponded to the pressure at altitudes of 6,000—8,000 m above sea level. Establishing these degrees of rarefaction (ascents) took from 55 sec to 6—7 min in various experiments, averaging about 2 min. After 30 sec of constant rarefaction (plateau) the pressure was brought back to the initial pressure in 1—2 min, i.e., sea level pressure (descent). In a number of experiments the descent was carried out much more quickly (in 3—7 sec) by means of a special adaptation. The animals were prepared for the experiment in the same way as in the short-term experiments of the previous series. In 56 ascents the animals breathed air, and there existed the possibility of brief anoxia occurring. During the other 114 ascents oxygen was used, thus eliminating the possibility of anoxia complicating the effect of expansion of the gas in the gastrointestinal tract. Evidently, there was no essential difference in the results of the experiments performed with and without oxygen, because of the brief stay at altitude.

With ascent to altitude the pressure in the gastrointestinal tract increased by 13—136 mm Hg over the barometric pressure in the chamber, and it dropped to the pressure level in the chamber on the plateau during the descent. Not uncommonly, this drop occurred in a stepwise manner, which was caused by belching and passage of gas through the rectum.

In all experiments the respiratory and blood pressure reactions were demonstrated distinctly and almost unitypically but to different degrees (Figure 3). These reactions resembled the changes described above after introduction of gas under considerable pressure. The greater the rate and magnitude of the pressure drop, the greater the reaction. Usually the reaction began shortly after the beginning of the ascent and at the beginning of the plateau period. Even before descent began the respiration and blood pressure began to return to the initial level. In the absolute majority of the experiments (21 out of 23) a slowing of respiration was noted to the point of brief apnea and reduction of the amplitude of the respiratory movements. Not uncommonly, respiration became irregular, and inspiration was markedly prolonged. In some experiments apnea lasted 10—17 sec. In a number of cases the blood pressure increased; in others it decreased to different degrees, but there was always a reduction in the size of its respiratory waves. Sometimes the size of the pulse waves was reduced and the heart rate slowed up. During the descent respiration and blood pressure returned to the initial level. However, all 5 cases of more rapid ascents (in 3—7 sec), carried out with 4 animals, resulted in marked dyspnea, in 2 cases, to a second distinct rise in the blood pressure.

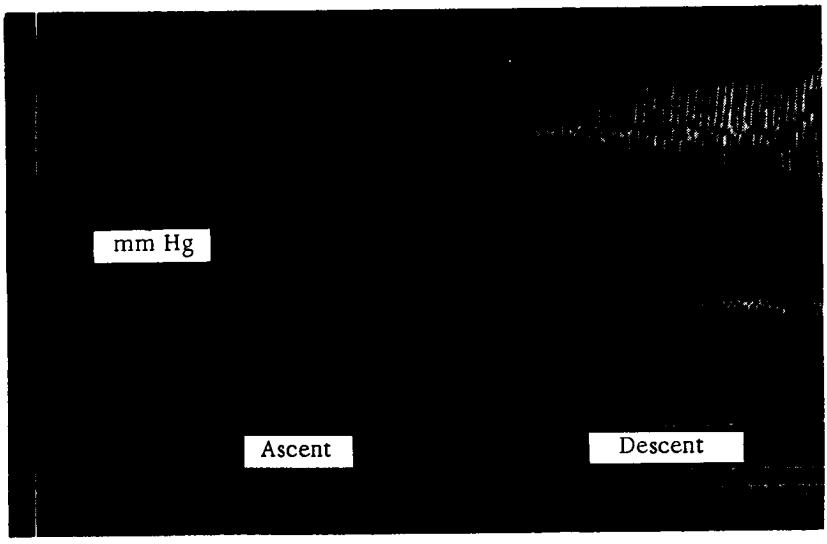


FIGURE 3. Changes in respiration and blood pressure in a dog with ascent to 6000 m. Experiment of 17 August 1949.

Tracing components (from top down): Respiration; blood pressure; base line of manometer; altitude marking; time marking.

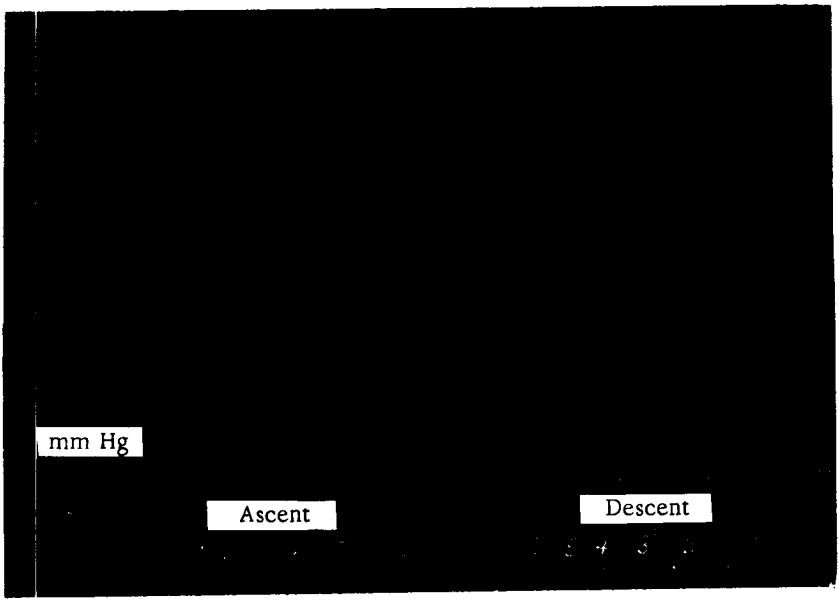


FIGURE 4. Absence or respiratory and blood pressure changes with drop in barometric pressure following novocain block of the vagus and splanchnic nerves and the abdominal nerve plexuses. Experiment of 17 October 1949.

The order of the tracing components is the same as for Figure 3.

In experiments performed after maximum preliminary removal of gas from the gastrointestinal tract the respiration and blood pressure either did not change at all with reduction of the barometric pressure, or the reaction was markedly lessened. Conversely, the ascents carried out after the additional introduction of air into the gastrointestinal tract were accompanied by a considerable increase in respiratory and blood pressure changes.

We then, as before, investigated the reaction to ascents after cutting and novocain block of the nerves and nerve plexuses. In all ascents with 2 animals, carried out after novocain block of the vagus nerves under the diaphragm, a considerable reduction of the respiratory changes and a lesser reduction of blood pressure changes were noted.

Cutting the splanchnic nerves caused a lesser change in the respiratory reaction and a greater change in blood pressure. In 4 cases there was no blood pressure reaction to the 7 ascents carried out after cutting the splanchnic nerves; in 1, the blood pressure rise was hardly noticeable and in 2 it decreased, whereas in the control ascents an increase in the blood pressure occurred.

Seven other ascents by two animals were carried out after bilateral novocain block of the splanchnic and vagus nerves and the nerve plexuses of the abdominal cavity. Of these, in 1 case there was no reaction (Figure 4); in 3 it was negligible; in the remaining 3, it was much less than in the control ascent. After the block of the vagus and splanchnic nerves and nerve plexuses had led to the disappearance of the respiratory and blood pressure reactions the novocain was washed out of the site into which it had been infiltrated. The ascents made after this were again accompanied by distinct respiratory and blood pressure reactions similar to those which had occurred before the novocain block.

Conclusions

1. Increase in the gas volume contained in the gastrointestinal tract with reduction of the barometric pressure causes a change in the frequency and depth of respiration, in the volume of pulmonary ventilation, the pulse rate, and in the strength of cardiac contraction and blood pressure.

2. The degree and nature of these changes depend on the pressure on the gastrointestinal wall developing with increase in the gas volume.

3. Respiratory and circulatory changes occurring from expansion of the gas in the gastrointestinal tract during a barometric drop depend mainly on the mechanism of visceral (interoceptive) reflexes from the mechanoreceptors of the stomach and intestines, and to a much lesser degree on the mechanical effects on the diaphragm, the position of the heart, and the lumina of abdominal vessels. The vagus and splanchnic nerves and nerve plexuses of the abdominal cavity participate in the realization of these reflexes.

4. The nature and physiological mechanism of the reactions to gas expansion in the gastrointestinal tract in the presence of barometric pressure drops should be taken into consideration in the prevention and the elimination of decompression disorders under conditions of high-altitude flights and emergence from underwater dives.

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CASE OF LATE MANIFESTATION OF INTRAPULMONARY PRESSURE

(Sluchai pozdnego proyavleniya barotravmy legkikh)

The cases of intrapulmonary pressure trauma with arterial gas embolism encountered in diving practice occur chiefly when the diving suit and diver's self-contained gear are used, wherein the person's lungs and the breathing bags of the apparatus represent a single "apparatus-lung" system.

The case of late manifestation of intrapulmonary pressure trauma being described is of interest to physicians specializing in physiology and to diving specialists, and should be taken into consideration in their practical activity.

On 1 February 1960 a group of divers using self-contained diving gear were surfacing from a depth of 18.5 m with a stop 13.5 m from the bottom. One of the light divers had opened the regulating outlet valve of the apparatus and dived after washing out the apparatus with oxygen three times as is required. After rising 2—3 m he felt considerable buoyancy, but held firmly to the buoy rope with his legs and arms and climbed up slowly. The diver released the gas mixture from his breathing bag from time to time through his nose into the space under the helmet; however, the buoyancy increased rapidly. Not being able to maintain himself any longer, he began to float up rapidly, sliding along the buoy rope. At 13.5 m he experienced a "clouding" of consciousness, and becoming separated from the buoy rope, rose precipitously to the surface. He was pulled out by the instructors responsible for the safety of the dives, pulled over the rope ladder, and then he got onto the platform by himself. The GK-2 diving suit was markedly inflated in its upper portion (down to the waist), and the regulation outlet valve in the helmet was closed by the neck strap of the apparatus. The breathing bag was also inflated. The diver's mouthpiece remained in his mouth.

The diver was quickly undressed. He offered no complaints; he felt good. There were no objective signs of sickness.

After completion of his duties the diver was again examined by physicians. His condition was good; skin and visible mucosae were normal. The pulse was 58 per min, rhythmical, of satisfactory quality. The heart borders were within normal limits; heart sounds were pure. The blood pressure was 110/70. The lungs were clear to percussion. Respiration was vesicular. Reflexes were lively and moderate.

The morning after the dive (16—18 hrs later) the diver felt pains in his chest on deep inspiration and then muscular pains in the area of the arms and chest. In the course of time his condition deteriorated: he developed

headache and dizziness, weakness, dyspnea, palpitation, and "throbbing" of his temples on mild physical exertion; however, he did not seek medical aid. Only more than three days after the dive did the diver come to the internist.

On examination no objective signs of pressure trauma were found. The temperature was 37°; the blood pressure, 140/85—140/90. He was relieved of duty for two days because of his state of health.

The next morning, after a second consultation, a survey X-ray film was made of his chest; the film showed indistinct shadows of a gas layer in both supraclavicular areas between the muscles; on the right these were in the form of a triangle and on the left, in the form of a strip. The headache, muscle pains, and dizziness continued.

On the basis of subjective complaints and roentgenographic findings a diagnosis of intrapulmonary pressure trauma was made, and the patient was placed in a recompression chamber with a physiologist for therapeutic recompression.

On 5 February at 12:20 p.m., i.e., 92 hrs after the dive, recompression was begun. A pressure of 8 atm was created for 20 min. At the end of the 30 minute period under this pressure the chest and muscle pains, headaches and dizziness lessened considerably. After the pressure had been reduced to 5.5 atm (1st stop) all the pathological signs disappeared. Subsequently, treatment was conducted according to routine IV of therapeutic recompression for intrapulmonary pressure trauma (PVS-58). To exclude the possibility of pneumonia developing during therapeutic recompression, the patient was given an intramuscular injection of 100,000 IU of penicillin every 4 hrs (total dose, 400,000 IU) and one tablespoon of a 10% $CaCl_2$ solution.

After emerging from the chamber the patient complained only of weakness and very slight chest pain on deep inspiration. The examination showed the following: pulse 64 per min, rhythmic, and of satisfactory quality; heart sounds pure and clear; blood pressure 120/60; vesicular respiration normal; body temperature 36.2°C; reflexes lively and moderate; cranial nerves showed no abnormality.

The patient was hospitalized, given penicillin injections, and oral administration of $CaCl_2$ and Vitamin C and B_1. A recheck X-ray film, made three days after therapeutic recompression, showed that there were no focal or infiltrative changes in the lungs; the heart was normal and there were rhythmical contractions. The aorta was normal. The pulse was 72 per min, of satisfactory quality; the blood pressure was 115/55. The heart sounds were pure. Respiration was normal vesicular.

After six days the patient was discharged from the infirmary in good condition.

The compression of the regulation outlet valve on the helmet had been a factor contributing to the occurrence of intrapulmonary pressure trauma.

As the result of the diver's rapid rise to the surface the pressure in the apparatus-lung system decreased to a lesser degree than the ambient pressure (the mouth-piece had stayed put). The outlet valve of the breathing apparatus had been opened and was in good working order, and because of its capacity could have provided for the discharge of the excess gas mixture. The increase in intrapulmonary pressure under these conditions might have been caused by laryngospasm. However, in

such a case pronounced clinical manifestations of spasm, inability to carry out inspiration or expiration, asphyxia and severe pain, etc. would have occurred. In view of the absence of these symptoms the reason for the increase in intrapulmonary pressure apparently lay in the fact that during the time the diver floated to the surface the mouthpiece did not leave his mouth, and the oppression of his tongue against the front teeth could have almost completely prevented the escape of the expanding alveolar air from the lungs. The resulting increase of air pressure in the lungs could have caused the pressure trauma. "The clouding of consciousness,"" during ascent to the surface was an expression of pressure trauma.

A characteristic feature of this case is the very late manifestation of signs of pressure trauma. Analysis permits us to draw the following practical conclusions.

1. The first signs of intrapulmonary pressure trauma (such as chest pains, dizziness, and headache) can occur several hours after the dive rather than in the first few minutes if there has been very slight injury to lung tissue. Therapeutic recompression should be conducted in all cases of intrapulmonary pressure trauma, regardless of the time at which it is demonstrated.

2. All cases in which divers shoot to the surface rapidly during training and regular diving work should be investigated carefully and repeatedly by physiologists, even in the absence of subjective complaints by the divers or objective signs of injury to lung tissue (cough, chest pain, hemoptysis, etc.). Since the diagnosis of such cases offers considerable difficulty, additional methods of investigation, chiefly roentgenography of the chest, should be used.

If, as the result of the investigation, pressure trauma is ruled out, the patient should be warned that with the appearance of even very slight malaise he should immediately go to the physiologists [the actual word here is "physician-physiologist"].

3. In carrying out training and regular diving work using diving equipment it is essential to pay special attention once again to preventing rapid ascent of the light diver to the surface. The rate of rise along the buoy rope should not exceed 10—15 m/min.

In cases where the diver cannot prevent rapid rise to the surface he should eject his mouthpiece and make a complete expiration.

N66-17161

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SEVERE SPINAL FORM OF DECOMPRESSION SICKNESS WITH A FAVORABLE OUTCOME

(Tyazhelaya spinal'naya forma dekompressionoi bolezni s blagopriyatnym iskhodom)

The rare cases of spinal form of decompression sickness encountered in divers deserve careful study. In the past 12 years four divers were sent to the Clinic of Nervous Diseases of the Military Medical Academy im. Kirov, for treatment of spinal cord lesions in decompression sickness. One of these cases was distinguished both by the conditions of occurrence and the characteristics of the course of the sickness.

The diver had suffered a very severe spinal form of decompression sickness in the acute period, complicated by a pulmonary lesion, burns on the body, bedsores, and cystitis. Despite this, the outcome was quite favorable because of comprehensive and prolonged treatment.

The distinctive nature of the occurrence and course of the disease in this case is, we believe, associated with certain individual characteristics of the diver.

We should like to give a brief description of the circumstances of the occurrence and course of the sickness in diver A. who underwent planned training in a recompression chamber on a training ship for divers.

Three divers, healthy according to all signs, entered the chamber at 2:19 p. m., and the pressure was raised to 6 atm in 8 min. They remained under this pressure for 21 min, after which the pressure was reduced to 1.8 atm. Subsequently, decompression was carried out according to schedule. During the pressure rise the divers felt well.

After 3—2.5 atm of decompression diver A. felt pain in the neck region and formication in the lower extremities. However, he ascribed no importance to this, considering these sensations to be the result of the uncomfortable position of his body in the chamber. After changing his position the pains and paresthesias disappeared, but a feeling of a certain degree of numbness of the lower extremities persisted until the end of decompression.

After the completion of the training session two divers felt well, and did not complain of anything. Diver A. noted severe constricting chest pains and a reduction of sensitivity in the lower half of the body immediately after emerging from the chamber (at 4:30 p. m.). At the same time, weakness in the lower extremities caused him difficultues in emerging from the chamber.

At 5:25 (i. e., 55 min after leaving the chamber) A. was again put into the chamber for therapeutic recompression. The elevation of the pressure

to 1.5 atm led to a considerable improvement in his condition, and at a pressure of 3.0 atm the symptoms of decompression sickness disappeared: the diver stated that he felt well, made movements with his upper and lower extremities in the chamber, and at 6:10 p.m. he ate supper.

Decompression was carried out without any deviation from the prescribed routine. However, at 10:35 p.m., during his stay under a pressure of 0.9 atm, his condition deteriorated markedly: pain developed in the chest, and there was a numbness of the skin of the lower extremities, trunk, neck, and occiput. The pressure was raised to 5.0 atm. No improvement occurred in the diver's condition; he developed signs of paralysis of the lower extremities. At 11:26 p.m. the pressure in the chamber was raised to 7.0 atm. In accordance with the routine, following a 50 minute stay under a pressure of 7.0 atm, it was reduced to 5.5 atm. No changes were noted in the patient's condition.

Upon arriving at the scene of the accident at 12:11 a.m. the physiologist found that the lower extremities were paralyzed and that there were signs of a pulmonary lesion. On his advice, the pressure was again raised to 7.0 atm, then to 8.0, and even to 9.0 atm. No improvement occurred in the patient's condition. At the maximum pressure, signs of pronounced nitrogen anesthesia developed. The subsequent therapeutic decompression was carried out according to a special routine (No. 8) with an increase in the final stages by 2—3 hrs. There was improvement in the patient's condition. At 3:05 a.m. the diver, making an attempt to turn over, fell out of bed, and because of the paralysis of his lower extremities, could not get up and remained lying on the hot deck). Measures were taken for setting up equipment so that the physician could enter the recompression chamber (a rescue ship went to a plant where an air lock was made and attached to the chamber hatch).

At 8:10 the physician entered the chamber; here he diagnosed paralysis of the lower extremities, paresis of the upper extremities, pulmonary infarctions, complicated by bilateral pneumonia and extensive second—third degree burns of the buttocks, sacrum and scapula (as the result of lying on the hot deck. The physician applied dressings to the burns, catheterized the patient (because of urinary retention), injected tetanus antiserum, camphor, caffeine, pantopon, penicillin (a total of 800,000 IU) and streptomycin (500,000 units).

Decompression was completed at 5:50 a.m. on 22 November; the patient was brought out of the chamber and sent to the hospital.

The patient's condition was serious. The pulse rate was 100, and the pulse was rhythmical. The heart sounds were considerably muffled. There were a large number of dry and moist rales in the lungs; there was constipation and urinary retention.

There was a second—third degree burn of 15 × 18 cm on the skin of the left buttock; in the scapular regions second degree burns of 7 × 12 cm and 2 × 5 cm. The total area of the burns was 350 sq. cm (5% of the body surface). On the skin of the right buttock there was a first degree burn, 10 × 5 cm, with uneven edges.

Neurological status. The patient was conscious, and showed no speech disorder. A nonpersistent horizontal nystagmus was found. The functions of the other cranial nerves were intact. The upper extremities showed no signs of paresis. Reflexes in the upper extremities were lively and equal on both sides. All types of sensation were reduced in the

right upper extremity in the area of segments C_7—C_8 The abdominal reflexes were markedly reduced; it was possible to elicit only the upper abdominal reflexes. The patient showed an intense paraparesis of the lower extremities; only very slight movements of the toes and ankle joint on the left were possible. On attempting to move the other joints, a barely noticeable contraction of the musculature of the lower extremities was observed. The tone of the lower extremities was reduced, particularly on the right. The knee and ankle reflexes were absent. There were bilateral Babinski signs and an Oppenheim sign on the right, and hypalgesia downward from the D_6—D_8 levels on both sides, which gradually changed to analgesia in the lower segments. A disorder of heat sensation also existed in the same area. Touch, two-point touch and proprioceptive sensation were intact.

Therefore, the history of the sickness and the objective findings after completion of therapeutic recompression permitted the diagnosis of a severe form of decompression sickness with involvement of the spinal cord (the main focus was at the D_6—D_8 level, and there were scattered foci in the upper thoracic and cervical segments), complicated by bilateral bronchopneumonia and second—third degree skin burns. The possibility that there were small pulmonary infarcts was not ruled out.

What caused the severe illness in diver A.? A study of his diving and medical records showed that there had been no violations of the decompression routine after the diver had been in the chamber at a "depth" of 60 m. This is also evidenced by the absence of disorder in the other two divers who had been in the chamber with the patient. Therefore, the reasons for the occurrence of caisson sickness during the decompression must be connected the individual characteristics of the patient or with the random localization of gas bubbles in the spinal cord.

During 1959, Diver A. had participated constantly in diving operations, although these were in shallow water (the greatest depth had been 31 m), and had spent 143 hours in diving practice. Therefore, it was hardly logical to consider that the predisposition of diver A. to decompression sickness was related to his insufficient training for being under higher pressure. Undoubtedly the delayed onset of therapeutic recompression (after 55 min) contributed to the development of the severe form of the sickness; therefore, subsequent proper treatment could no longer assure the diver's complete cure.

As has been mentioned, the condition of the patient upon hospitalization was serious. The fact that in transverse lesions of the spinal cord trophic disorders of the skin occur, indolent decubiti appear, and that infection of them can cause sepsis was worrisome. The second danger for such patients is constituted by urinary tract complications, because pyogenic infections can develop in connection with urinary disorders and the need for frequent catheterization.

In this case prognosis was made worse by the fact that involvement of the spinal cord was combined with a disease of the lungs (bronchopneumonia) and burns (undoubtedly infected). Only comprehensive and vigorous treatment for a long period led to the elimination of the complications and considerable recovery of the loss of spinal cord functions. Beginning with the first day, antibiotics were prescribed for the patient (penicillin and streptomycin); he was given cardiac agents (camphor, coramine and

caffeine); Vitamins C, B_1, and B_{12}, strychnine, prostigmine, and calcium gluconate, as well as blood transfusion, and infusion of physiological saline solution.

On 29 November the patient developed mild active movements in all the joints of both lower extremities. The next day he developed an allergic reaction with pronounced urticaria, edema, and swelling of the joints. Diver A. still has urticaria at times, but it has occurred in a milder form. We want to draw attention to this characteristic of the patient, which, we believe, played a part in the pathogenesis of the decompression sickness which developed. Penicillin and streptomycine were stopped, and tetracycline, benadryl and calcium chloride were prescribed. On 3 December the urticaria disappeared.

On 4 December massage and passive gymnastics for the lower extremities were prescribed. On 8 December a necretomy of the burn surface was performed in the area of the left buttock.

On 16 December the patient's condition deteriorated. The temperature was 38.3°. A right-sided bronchopneumonia was diagnosed. Sulfathiazole and streptomycin were again prescribed. By 6 January the infiltration of the right lung had disappeared, judging by the X-ray film, and the fever had become low-grade.

By 19 January the range of active movement in the lower extremities had increased to such a degree that the patient was permitted to get out of bed three times a day and to take several steps near the bed.

On 27 January streptomycin was stopped; the next day an allergic reaction recurred with urticaria and elevation of the temperature to 39.0; by 3 February multiple itching hives appeared, and the patient could not urinate because of edema of the prepuce. Catheterization was performed and calcium chloride and benadryl were given followed by prednisolone and calcium chloride.

On 4 February the urticaria disappeared but on the next day the patient developed a chill and in the evening had a temperature of 40.5°. He passed a large quantity of bloody urine. A diagnosis was made of cystopyelitis and a septic state. A Staphylococcus albus insensitive to penicillin, aureomycin, levomycetin [laevo-rotary chloramphenicol] and streptomycin was isolated. On cystoscopy signs of acute hemorrhagic cystitis were found. A second course of tetracycline treatment was begun (200,000 units four times a day).

On 25 February 1960 the patient was transferred to the Clinic of Nervous Diseases of the Military Medical Order of Lenin Academy im. Kirov.

The following is the abstract of his case history, No. 1402/727 (clinic).

Neurological examination: pupils regular, reaction normal; mild nystagmoid jerks of the eyeballs on extreme deviation; the other cranial nerves were normal.

Upper extremities showed no signs of paresis; the abdominal reflexes could not be elicited. The knee and ankle jerks were very active, more on the right side; ankle and patellar clonus was found. Muscle tone in the lower extremities was increased. Positive Babinski, Bekhterev, Rossolimo, Zhukovskii, Oppenheim and Gordon signs were observed on both sides. Active movements were made satisfactorily in all joints of the lower extremities but they were weak; dorsiflexion of the feet was particularly difficult. The extended lower extremities could be raised above the bed at an angle of 45°. The patient could walk if he held on to nearby objects.

There was analgesia and temperature anesthesia of the feet and legs (as high as the knee joints) and a reduction of the same types of sensation on the thighs. Proprioception and touch sensation were intact. Pelvic functions: periodic urinary incontinence with signs of cystitis and constipation.

The heart borders were within normal limits on percussion; heart sounds were pure; pulse was 88 per min; blood pressure 120/80 mm. The breathing sounds in the lungs were vesicular. The abdomen was soft and tender in the gall bladder region.

On the left buttock there was a clean granulating wound 9 × 8 cm in size. In the area of the greater trochanter on the right there was a decubitus of 3 × 4 cm with necrosis of the skin. Somewhat above it there was a small fresh decubits, 1 × 1 cm.

The patient was treated in the clinic from 26 February through 1 July. In this time his condition improved considerably. Before discharge he walked about freely without a cane and climbed three flights of stairs by himself; his urination had become normal and he was not troubled by constipation. The decubiti and burns healed. The signs of cystitis were eliminated.

During his stay in the clinic the patient was given varied drug treatment, including antibiotics, nystatin (because of aphthous stomatitis), vitamins, injections of aloe, protigmine, dibazole, and others, as well as massage and therapeutic gymnastics for the lower extremities.

He was discharged on 1 July with mild residual signs of a spastic paraparesis of the lower extremities and reduced sensation on the skin of the lower extremities. The internal organs showed no pathological features; blood and urine analyses were normal. The patient went to the sanatorium by himself for further treatment.

In conclusion we should like to dwell once again on a characteristic feature of the case described: the patient was predisposed to allergic reactions from various causes, expressed in urticaria, mild edema, and joint pains. The occurrence and severity of the decompression sickness in diver A. (while his two comrades remained well under the same conditions) are apparently explained not only by air embolism of the spinal cord but also by the appearance of extensive edema according to the mechanism of an allergic reaction. The combination of these pathogenetic factors were responsible for the high degree of spinal cord involvement in the initial period, which was aggravated by the late onset of therapeutic recompression. Elimination of the reactive edema led to a very great recovery of the spinal functions. We have not seen such a definite recovery from the disorders in cases of "pure" air embolism of the spinal cord in decompression sickness. The relatively favorable outcome of the sickness permits us to believe that in this case the spinal cord involvement was caused not only by foci or necrosis but also by the edema and other reversible vasomotor disorders.

On the basis of the etiological analysis of this case, we would call the attention of physicians selecting candidates for diving work and observing their state of health to the need for a careful study of the autonomic-vasomotor functions, and, particularly, the detection of persons with a tendency toward vasomotor-allergic reactions.

N66-17162

G. L. Zal'tsman, I. D. Zinov'eva, and S. D. Kumanichkin

INCREASED INDIVIDUAL PREDISPOSITION OF A SUBJECT TO THE EFFECT OF HIGH PARTIAL OXYGEN PRESSURE

(O povyshennoi individual'noi predraspolozhennosti ispytuemogo k deistviyu vysokikh partsial'nykh davlenii kisloroda)

As is well known, one of the signs of the toxic effect of increased oxygen pressure may be concentric constriction of peripheral visual fields, usually regarded as the result of spasm of the retinal vessels. However, this disorder was noted only after the prolonged effect of high partial oxygen pressure. Thus, Behnke, Forbes and Motley (1936) described such constriction in subjects after a three-hour stay under a pressure of 3 atm of pure oxygen.

Under the influence of lower oxygen pressures used for ordinary diving work, such a disorder has not been described. In 1959, we made a special measurement of peripheral visual fields of 10 divers before and after descent to different depths in a recompression chamber. Using a perimeter and the generally accepted method, no pronounced changes in the peripheral vision were found.

In only one subject was it possible to observe a considerable concentric constriction of peripheral visual fields. In 1954, N. T. Koval' and V. V. Smolin had noted a brief loss of vision in this subject after a dive to 100 m under marine conditions. However, no special study was made. In subsequent years the diver participated in dives to depths of up to 100 m and did not notice any pronounced visual disorders. He was not permitted to participate in dives in which high partial oxygen pressures were used for a long time.

In the case being described the diver participated in a "descent" in a dry pressure chamber with a maximum pressure of 120 m H_2O. He remained at this pressure for 30 min with subsequent long-term decompression for 5 hrs and 38 min. During the period spent under maximum pressure and in the initial stage of decompression to the 60 m level, the diver breathed an enriched air-helim mixture (13% oxygen, 25% nitrogen, 62% helium) and then air; beginning with a 20 m stop, pure oxygen. A barogram of partial oxygen pressures during the descent is shown in Figure 1, I. At the 14 m level, 57 min after switching over to breathing pure oxygen, the diver had a "screened shroud" before his eyes, particularly the right. With further reduction of the pressure this sensation decreased somewhat; however, it remained even after the conclusion of the decompression. Three minutes after emerging from the chamber the diver was examined with the use of a perimeter. A considerable concentric

constriction of the peripheral visual field was found, from which the patient recovered almost completely after 40 min (Figure 2, I).

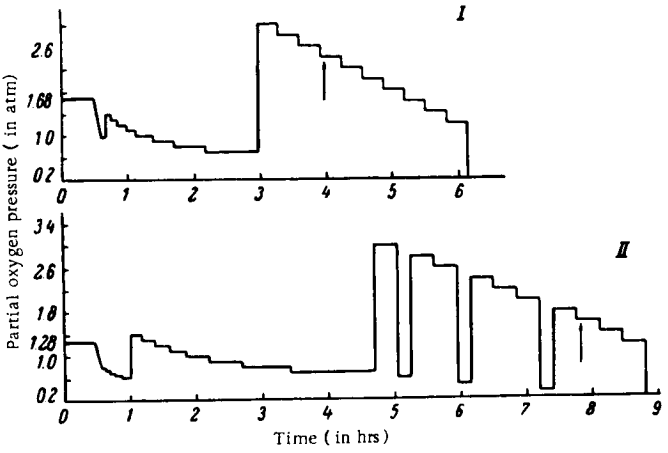


FIGURE 1. Barogram of partial oxygen pressures in the deepwater diving routines used

I—routine of 120 m for 30 min of continuous oxygen decompression; II—routine of 140 m for 30 min of oxygen decompression, with three intervals using air. The arrow designates the time of occurrence of the subjective visual changes.

As experimental data on animals show (Lembertsen, 1955), an effective method for reducing the toxic effect of oxygen is to create intervals in which air is used during the breathing of pure oxygen under pressure. These "air interruptions" of the oxygen phase of decompression began to be used in diving practice also, on the suggestion of Z. S. Gusinskii and V. V. Smolin. In this connection, it was interesting to check the effectiveness of "air interruptions" in the oxygen phase of decompression of the same diver.

A descent was carried out in a pressure chamber with a 30 minute stay under the maximum pressure of 140 m H_2O and subsequent decompression for 8 hrs and 18 min. During the period under maximum pressure and in the initial stage of decompression to the 60 m stop, the diver breathed a helium-oxygen mixture (8.5% oxygen), then air, and, beginning with the 20 m stop, pure oxygen. During oxygen decompression 3 "air interruptions" were made, 14 min each. A barogram of the partial oxygen pressures is shown on Figure 1, II.

During the course of decompression at the 10 m stop 2 hrs and 9 min after switching over to breathing oxygen, the diver also developed a sensation of a "small screened shroud" before his right eye, which was maintained during the entire subsequent decompression. Three minutes after emerging from the chamber the diver was examined with the use of a perimeter. A concentric constriction of the peripheral visual field of the right eye was found (Figure 2, II). After 50 min his vision was recovered completely.

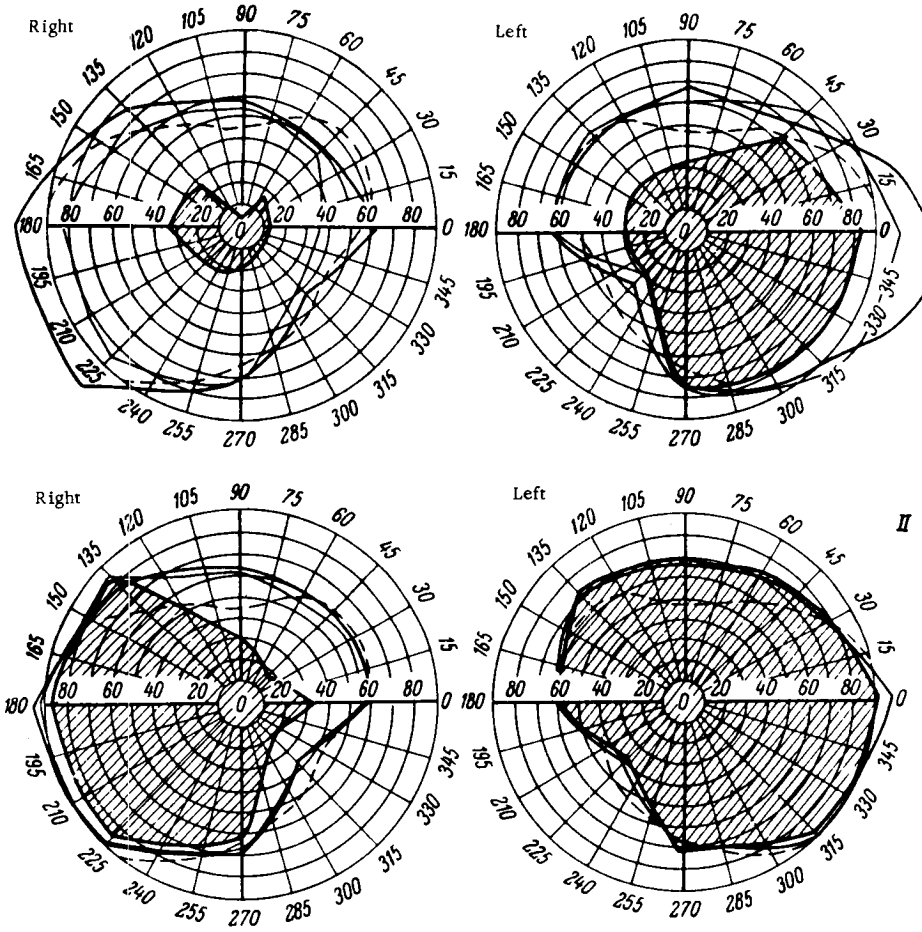


FIGURE 2. Results of determination of peripheral visual field of a diver before and after a "deep-water" dive in a dry pressure chamber

I—with ordinary oxygen decompression; II—with oxygen decompression and three intervals with air.

On comparison with previous studies, constriction of the peripheral visual fields appeared in only one eye and was much less pronounced; it disappeared completely, despite the long period of oxygen decompression (210 instead of 190 min). It should be noted that subjective sensations appeared in the last descent to a lesser degree and at later periods after switching over to breathing oxygen (after 129 instead of 57 min).

Conclusions

1. Persons with greater individual predisposition to the action of high oxygen pressures may be encountered among divers. This indicates the need for working out the method for making a specific medical selection

of the divers. One of these methods may be the determination of the peripheral visual fields after the use of increased oxygen pressures.

2. The case presented showed the expediency of using "air interruptions" during oxygen decompression with the aim of reducing the toxic effect of oxygen.

Bibliography

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